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PERIPHERAL VASCULAR GRAFTS*

EXPERIMENTAL COMPARISON OF AUTOGENOUS VEINS, HOMOLOGOUS ARTERIES, AND SYNTHETIC TUBES

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COMPARISON of the various materials available for vascular grafting for peripheral atherosclerotic occlusion is difficult because of the lack of control of clinical series, difficulty in follow-up of patients, and inability to separate the results of progression of the basic disease from changes in the grafting materials. Reports of laboratory experience are relatively few, although such appears to offer a means of comparing the various materials, since normal dog experiments avoid most of the disadvantages cited above in clinical cases. The experimental data reported to date have largely been concerned with aortic grafting, which is admittedly easy to accomplish no matter what material is chosen. Harrison (1957 a), for instance, reported only 1 failure in 84 canine aortic grafts using various synthetics, and experience in this laboratory agrees with this. Only a few experimental peripheral vascular grafting procedures have been reported and most of these failed.

Attention was turned to the problem of peripheral vascular grafting in this laboratory in 1953, although other investigators here had experience with aortic replacement dating back to 1949. In the five years of experimental peripheral grafting in dogs it has become apparent that the procedure can be accomplished with any of several materials, but that peripheral grafting in the dog is more difficult than is aortic grafting and that it is a more severe test of any material. The experience reported herein shows that in comparable series of peripheral replacements by autogenous veins (Jones and Dale, 1958), homologous arteries (Mavor, 1956), and various synthetics (Dale and Niguidula, 1958), the latter have considerably less chance of remaining patent than either the

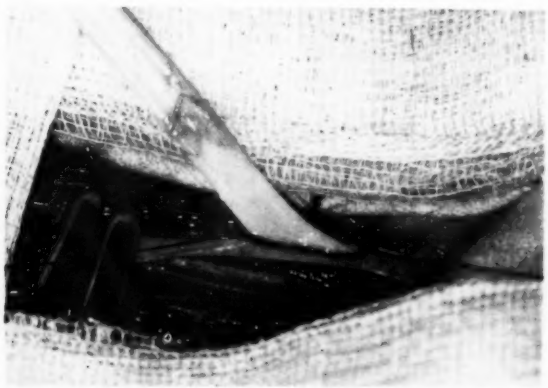

FIG. 327.—Completed anastomosis between autogenous vein and femoral of dog to indicate continuous over-and-over 5–0 silk suture line broken at each end by interrupted mattress sutures. The relation of the tiny through-and-through tissue bites to the surgical sponges is apparent.

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autogenous vein or the homologous artery under these severe test conditions. It appears that from the standpoint of the graft itself, either autogenous veins or homologous arteries are preferable for small peripheral vessels.

METHODS

Operations were performed under intravenous nembutal anæsthesia, using a technique similar to that employed in the clinical operating room. Silk in 4–0 and 5–0 size was used for all sutures and every

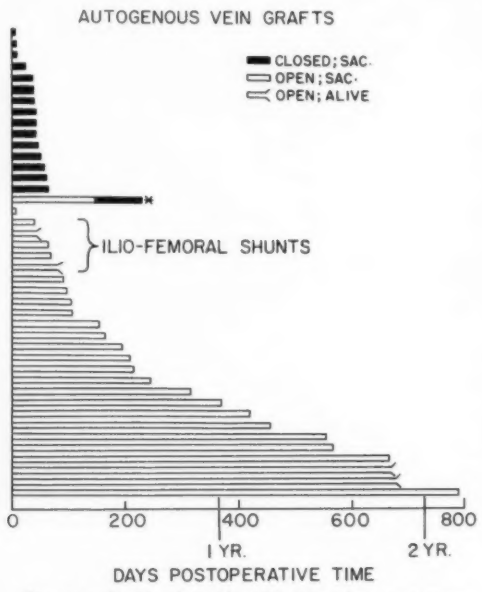

FIG. 328.—Results of experimental series of 42 autogenous vein grafts.

attempt was made to manage tissue with sharp, delicate, and aseptic technique. No antibiotics were given following operation unless the chest had been opened, in which case a daily intramuscular injection of procaine penicillin was used.

Although some of the earlier arterial grafts were placed with everting technique, the later ones and all of the veins and synthetics were placed with over-and-over continuous suture, using a mattress stitch at either end of the incision to evert and to break the continuous suture line. Anastomoses were performed in end-to-side fashion, making the stoma larger than the lumen of the host vessel (eventually reaching a size where the length of the arterial opening was three times the diameter of the host vessel). *Fig.* 327 shows details of a completed end-to-side autogenous vein graft.

Homologous arteries were obtained from dogs sacrificed in this laboratory for other purposes. They were taken from the animal with aseptic technique, cultured and stored in a penicillin and streptomycin solution for twenty-four hours at 4° C. and until a negative culture returned, and then quickly frozen within an outer container of liquid nitrogen. Storage was then in the deep freeze at −20° C. Reconstitution was performed by returning the graft to room temperature and adding saline. All arterial branches were suture-ligated with 5–0 silk.

Autogenous veins were obtained from the same animal by exposing the saphenous vein lower down in the leg and carefully tying and dividing all tributaries. The vein was reversed to change the valve direction prior to placement as a shunt graft.

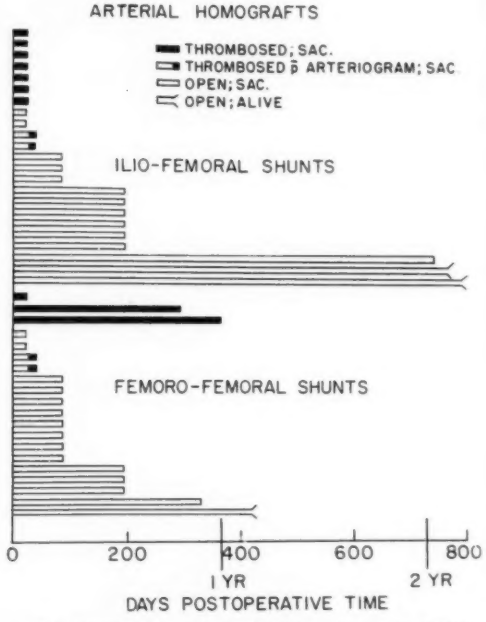

FIG. 329.—Results of experimental series of 43 arterial homografts.

Synthetic materials were uniformly boiled in detergent (Joy) for an hour and then washed in distilled water prior to sterilization in the autoclave. The brownish impurities coating the outer surface of Teflon were removed by boiling in concentrated sulphuric acid for a week prior to washing detergent. The actual cautery was used to seal the edges of both crimped nylon and 'Ethigraft' dacron tubes. Others were turned as a cuff or flange at the ends.

Arteriograms were performed at intervals to ascertain patency of the grafts. The animals were anaesthetized with intravenous nembutal and 14 c.c. of 35 per cent sodium acetrizoate (urokon) was injected percutaneously into the abdominal aorta or by a cannula passed up the contralateral femoral artery into the aorta.

Post-mortem examination was done either at the time when an arteriogram showed occlusion of the graft or at the time selected for sacrifice if the graft remained patent. Since it was not the purpose of this study to follow changes over an extremely long period, the majority of the animals were sacrificed relatively early. Post-mortem examinations were ordinarily limited to the area of the graft and vessels

in the vicinity. Microscopical sections were made of selected grafts and vessels.

RESULTS

Autogenous Vein Grafts.—*Fig.* 328 illustrates the overall result in 42 vein grafts, of which 16 thrombosed prior to sacrifice and 26 were either open at autopsy or by arteriogram at the post-operative date indicated. These vein grafts varied from 5 to 10 cm. in length and were invariably placed end-to-side between the proximal and distal superficial femoral artery except for five iliofemoral shunts. It was soon learned that placement of a saphenous vein graft into the dog's femoral artery required a considerably more delicate technique than did the placement of homologous arteries or synthetics. The majority of the thromboses indicated in *Fig.* 328 occurred early in the experience of the individual operator and in fact only 3 of the failures occurred after the operator had obtained his first success with the method. There was only 1 instance where an initially patent vein graft thrombosed later. Details of these vein grafts have been reported earlier (Jones and Dale, 1958).

Homologous Arterial Grafts.—*Fig.* 329 illustrates the 43 arterial homografts placed either as iliofemoral shunts or as shunts between the proximal and distal femoral arteries. This series is a small expansion of that reported earlier by Mavor (1956). Fourteen of these grafts thrombosed at one time or another while 29 remained patent. The 4 which thrombosed after an early arteriogram are in the doubtful category since it is not certain whether this was due to the urokon injection or whether the grafts would have thrombosed shortly in any event. In this homologous arterial series it should again be emphasized that the overall percentage does not necessarily reflect what should be expected of an experienced operator because all the figures show every animal that was employed no matter what the previous experience.

Synthetic Tubes.—*Fig.* 330 graphically illustrates experience with 68 synthetic tubes placed as grafts either between the aorta, the iliac or femoral artery, and a more distal vessel. Excluded are a series of 37 synthetic aortic grafts, of which 26 were successfully patent. Again, in this series of synthetics, the total experience is shown without selection. Six different synthetics were used. 'Fluflon' dacron proved to be the easiest material to place and suture and since it is a two-way-stretch fabric it conformed to the host bed better than any other. Its patency ratio was as good as any other synthetic. Crimped nylon was found to be somewhat more difficult to suture, particularly because the end-fibres tended to protrude into the lumen despite heat-sealing with the actual cautery. Crimped nylon also conforms to the host bed. Schlegal nylon was abandoned after early testing because it appeared that it had no particular advantage over the crimped nylon, which was more easily obtainable. Teflon tubes which were used a small number of times were somewhat more difficult to suture. The 'Ethigraft' dacron tube was easy to use except at the flange, where suture was somewhat difficult. Sheet orlon was used only a few times in the early experience. Details of these studies have been reported recently (Dale and Niguidula, 1959).

DISCUSSION

Total experience in this laboratory with autogenous veins, homologous arteries, and synthetic tubes placed as peripheral shunt grafts in dogs now amounts to 153 operations. This specifically excludes all aortic replacement operations. The experience of others (Harrison, 1957 a, b), as well as of this laboratory, indicates that the dog's aorta can be replaced by a variety of materials with a high expectation of success. Peripheral vascular grafting in the dog is, on the other hand, a much more difficult operation and the experience herein reported indicates that it is a much better differential test of grafting materials than is aortic replacement. Although it has been felt rather generally that the peripheral vessels of a dog were too small to permit any

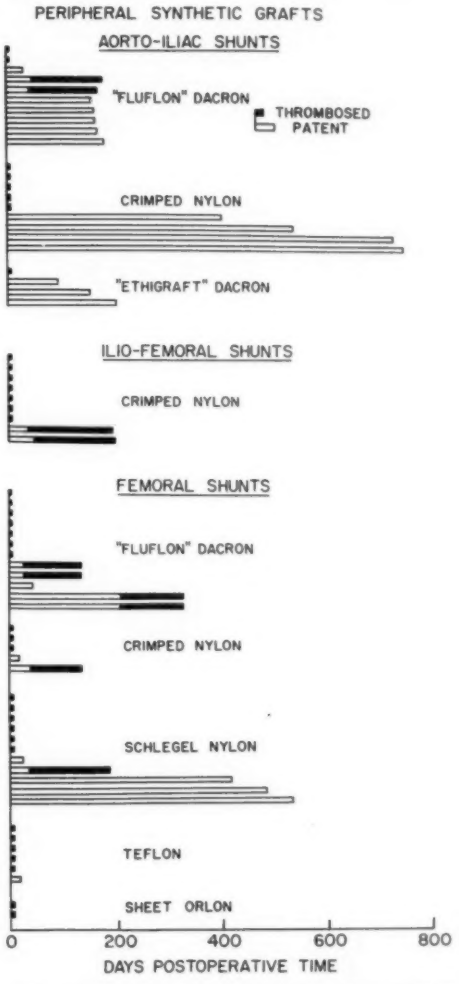

FIG. 330.—Results of experimental series of 68 synthetic grafts.

particular degree of success, our experience indicates that while this may be true for synthetic replacements, careful technique enables successful homologous arterial and autogenous venous shunt grafting in the dog's femoral arterial system. *Table I* is a comparison of the results of these 153 peripheral grafts in dogs. Reference to *Figs.* 328–330 indicates the time interval in each series. The overall patency rate for autogenous veins was 64 per cent, for homologous arteries 77 per cent, and for the total of the various synthetics 29 per cent. These percentages are based on every operation performed, and for intelligent interpretation require further correction. The arterial and venous grafts were performed prior to any of the synthetic grafts and so most of the learning process occurred during those operations.

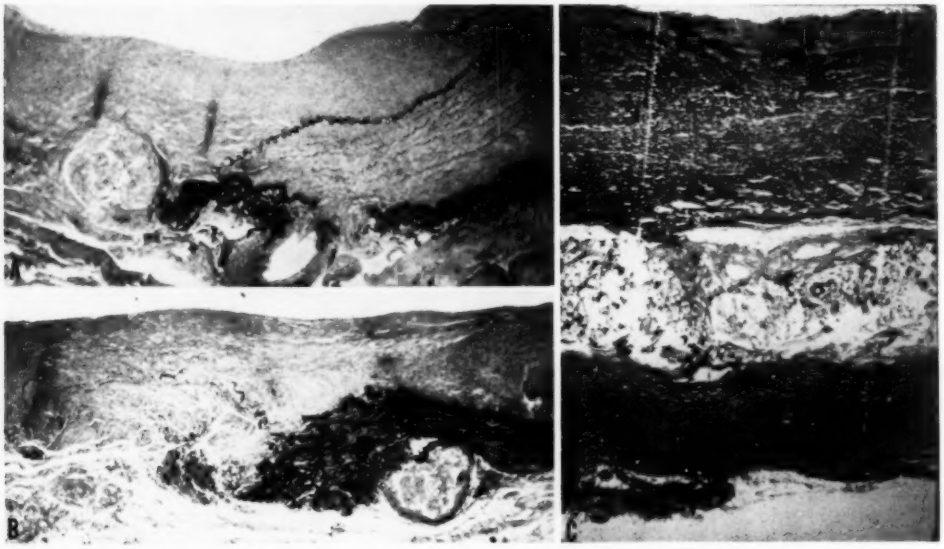

FIG. 331.—Microscopical sections of graft materials from dogs. A, Upper left, autogenous vein graft shows thickening. B, Lower left, homologous artery graft shows fragmentation of elastic fibres on left side while most elastic fibres on right are well preserved. Fibrosis of graft is evident. C, Right, shows central open and where 'Fluflon' dacron fibres lie with very thick fibrous neo-intima alone.

Table I.—COMPARISON OF 153 PERIPHERAL SHUNT GRAFTS IN DOGS

Graft	*No.*	*Patency (per cent)*
Autogenous vein	42	64
Homologous artery	43	77
Various synthetics	68	29

For instance, analysis of the autogenous vein grafts indicated that after the operator had successfully mastered the technique of placing the graft, there was every likelihood of success in any future operation. If the vein percentage is recalculated, starting with the first successful graft of the operator, it is found that 86 per cent of the autogenous veins remained patent. No such correction is possible for the synthetic graft series, and it appears that the 29 per cent patency shown in *Table I* is the best that could be accomplished in this laboratory using these materials. Further inspection of *Fig.* 330 also indicates that many of the successful synthetic shunts were placed between the aorta and an iliac artery and that the patency percentage for femoro-femoral shunts alone was extremely low (19 per cent of 36 operations). Thus, it can be seen that if the results of synthetic grafting to small vessels is compared to that for arteries and veins, the synthetics appear to be quite inferior. Peripheral grafting in the dog indicates the desirability of using either homologous arteries or autogenous veins if small vessels are to be shunted, because of the likelihood of failure using any of the synthetics listed.

The reason for poorer results with the synthetics as compared to arteries and veins appears to lie in the thickness of the pseudo-intima which eventually lines the inside of the synthetic tube. Whereas there was no late thrombosis in the artery and vein series (except in 4 instances where thrombosis followed arteriography), there were 10 proven cases where a synthetic graft was known to be open for a considerable period and later thrombosed. *Fig.* 330 indicates these as initially clear bars becoming solid later.

Microscopical study of the several materials used for grafting indicates that the autogenous venous graft persists as a living tissue. There is fibrous thickening of all layers of the autogenous veins, so that the venous wall increases in thickness. On the other hand, arterial homografts studied at long intervals after replacement often have the characteristics of fibrous tubes with broken elastic fibres and major changes in the smooth-muscle layer. There is no thickening of the wall of the homograft. The tendency toward replacement of the homograft by fibrous tissue and toward degeneration of its remaining tissue probably accounts for the reports of difficulties and complications with peripheral homologous arterial grafts in humans occurring as time

passes (De Weese, Wood, and Dale, 1959; Szilagyi, McDonald, and Smith, 1957). *Fig.* 331 compares the microscopical sections of a typical autogenous vein and homologous arterial transplant as well as a 'fluflon' dacron synthetic graft. The synthetic is notable for the thickness of the neo-intima layer which decreases the diameter of the lumen considerably. This has been pointed out and particularly discussed by Harrison (1957 a, b).

One of the chief difficulties in the use of any grafting material is the possibility of later dilatation and aneurysm formation. There appears to have been some confusion between the results of venous replacement of large arteries such as the aorta and of smaller peripheral vessels such as the femoral and popliteal arteries. Experimentally, the replacement of dog's aorta by autogenous vena cava results in a high incidence of aneurysm formation, as reported by Southgate, Foman, and Mahoney (1955). However, experimental and clinical results with autogenous veins used peripherally has indicated a very low or absent incidence of aneurysm formation. Indeed, the origin of the generally accepted idea that autogenous veins form aneurysms in a high percentage of instances is impossible to trace in the literature. Several explanations for the different behaviour of veins used to replace arteries of different sizes have been made. The most common explanation has been that when a vein is placed into the abdomen, the muscular and fascial support presented in the thigh is not available to prevent aneurysm formation. This, however, seems unlikely and a more probable explanation lies in a consideration of the LaPlace law,

$$T = PR,$$

where T is the tension in the wall, P is the excess hydrostatic pressure within the vessel over the pressure outside the vessel, and R is the radius of the vessel. As discussed by Burton (1951) and Barnett and Fraser (1955), the mean pressure within the vascular tree changes only three or four times from the aorta to the capillaries, whereas the radius changes by a factor of over a thousand times. The radius thus becomes the predominating factor in determining the total tension in the wall. It seems likely, therefore, that the tension T for a large aortic replacement such as the aorta is often great enough to cause dilatation and rupture of elastic or collagen fibres in the vein wall, but is not great enough to do this in the femoro-popliteal system. Thus, while dilatation and aneurysms are not unknown in peripheral vein grafts, they are uncommon, and in this experimental series did not occur during the period of observation, although there was often a slight degree of initial dilatation in the vein. There was no dilatation or aneurysm formation with any of the homologous arteries in this series, although such has been reported clinically and has occurred in our experience following the use of homologous arterial peripheral grafts in patients (De Weese, Wood, and Dale, 1958).

CLINICAL SURGICAL POLICY

Clinical practice in the University of Rochester Medical Center has been strongly influenced by this continuing series of experimental peripheral vascular grafts. Whereas initially homologous arteries appeared to be the material of choice for peripheral atherosclerotic femoral lesion replacement or shunting, reports of others (Szilagyi and others, 1957) as well as experience here (De Weese and others, 1958) have indicated that homologous arteries may degenerate over a period of time with

FIG. 332.—Arteriograms to illustrate clinical result using autogenous venous shunt graft. A, Irregularities in right superficial femoral artery which was not operated on. B, Arteriogram shows irregularities and multiple blocks of left superficial femoral artery. C, Shows autogenous venous shunt graft in place 22 days post-operatively following left shunt grafting. The diseased superficial femoral artery distally has become completely thrombosed while graft is patent.

dilatation and aneurysm formation as well as late thrombosis. Excellent laboratory experience outlined above with autogenous veins indicated a cautious clinical trial of such. Synthetic peripheral replacements have been used only occasionally because this experimental work indicates that a vein graft is more likely to be satisfactory when used to by-pass a small peripheral vessel. It is, of course, recognized that occasionally an autogenous vein may not be available and in such a situation a synthetic may prove to be a better choice than homologous artery because of the incidence of degeneration and aneurysm formation in the latter. For replacement of large vessels such as the aorta and iliac vessels a synthetic is, on the other hand, preferred, as indicated in *Table II*.

Since the change from a preference for homologous artery to autogenous vein for clinical peripheral vascular by-pass grafting which occurred in the Spring of 1957, there have been 28 autogenous

venous shunt grafts placed for atherosclerotic disease of the femoro-popliteal system. Twenty-one of these 28 have remained patent for periods varying between two weeks (the most recent one) up to over a year. Seven of the autogenous vein grafts have become blocked. All of these occurred in the immediate post-operative period and are thought to be due to either technical error or error in selection in that the candidate had a poor 'run-off' system resulting in an early graft thrombosis. While it was initially feared that the technique of autogenous venous grafting was so difficult that it would not be generally applicable, this has not proved so, and these grafts have been successfully placed by several different surgeons as well as by members of the resident staff. *Fig.* 332 shows the pre-operative and post-operative femoral arteriograms of a patient having a venous autogenous shunt graft thus shown to be patent 22 days post-operatively. To date no venous graft has dilated although the clinical follow-up is brief.

Table II.—CURRENT CLINICAL PREFERENCE FOR VASCULAR GRAFTING

	Great Vessel (Aorta and Iliac Artery)	*Peripheral (Femoro-popliteal)*
Preference:	Synthetic	Autogenous vein
Next best:	Homologous artery	Synthetic or
Avoid:	Autogenous vein	Homologous artery

On the basis of clinical experience with autogenous vein shunts, it may be that there is still some justification for the use of homologous artery in late cases of femoro-popliteal thrombosis where the lower leg vessels are grossly diseased or thrombosed. In such instances the use of a large calibre arterial homograft may have an advantage in the presence of the poor peripheral 'run-off'. Moreover such patients, who will have incipient or established gangrene, are generally in an old age group, 65–75 years, and usually have generalized atherosclerotic disease, so that quite apart from the limb ischæmia, life expectancy is limited and the possibility of homograft degeneration unlikely.

SUMMARY

1. In a series of 153 dogs subjected to peripheral shunt arterial grafting the results in terms of patency of both autogenous veins and homologous arteries were superior to those for various synthetic tubes. This appears to be due to the deposition of a relatively thick neo-intima in the synthetic tube which does not occur in either the autogenous vein or the homologous artery. These animal experiments, therefore, are considerably more critical for differentiating between grafting materials than is aortic replacement.

2. While dilatation and aneurysm formation is known to occur relatively frequently when a large vessel such as the aorta is replaced by autogenous vein, this is unlikely when the vein replaces a smaller peripheral artery because of the lower tension on the wall of the replacing vein.

3. The laboratory results have caused a change in clinical policy from the previous use of homologous arteries to the present use of autogenous veins for peripheral shunt replacement of atherosclerotic lesions of the femoro-popliteal system. Early results in 28 clinical patients have been satisfactory.

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SOME OBSERVATIONS ON THE CAUSE AND TREATMENT OF HARE-LIP AND CLEFT PALATE, BASED ON THE TREATMENT OF 1041 PATIENTS

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Incidence.—About 2 babies in every 100 arrive in this world handicapped by some sort of congenital abnormality. (Malpas, 1937; Coffey and Jessop, 1955.) The incidence of hare-lip and cleft palate is about 1 in 600 births. Boys are affected more often than girls, and the ratio is about 3 : 2 (*Table I*).

Table I.—Sex Distribution in All Types of Cleft Lip and Palate

	Male		Female	
	No. of Cases	Per-centage	No. of Cases	Per-centage
Fogh-Andersen (1946) : 1000 cases	606	60·6	394	39·4
Present series: 1041 cases	596	57·3	445	42·7

Ratio—Male 3:Female 2.

The incidence of hare-lip alone, of cleft palate alone, and of hare-lip and cleft palate together, is roughly 25 per cent, 25 per cent, and 50 per cent respectively (*Table II*).

In my series, however, cleft palate alone occurred half as frequently again as hare-lip alone, and the combined lesions accounted for rather less than one-half of my cases. Other congenital abnormalities were associated with the cleft lip or palate in 92 of the 1041 cases, i.e., 9 per cent.

Table II.—Incidence of the Different Types of Cleft in the Lip and Palate

	Veau (100 Cases)	Fogh-Andersen (1958)		Present Series	
	Per-centage	No. of Cases	Per-centage	No. of Cases	Per-centage
Hare-lip alone	25	928	32·2	233	22·4
Hare-lip and cleft palate	50	1289	44·8	450	43·2
Cleft palate alone	25	663	23·0	358	34·4

The sex ratio in cleft palate alone seems almost exactly the opposite to that of hare-lip alone (*Table III*).

Partial clefts of the hard and soft palate, without hare-lip, are much more common in girls (*Table III*), and represent a condition which is genetically distinct from the other types of cleft. They are inherited through a different gene and, when familial, occur in different families from the others. The shape of the cleft is also different; in the partial type there is a deficiency of soft tissue in front, whereas in the complete one there is just a separation. In the partial type, the cleft in front is U-shaped (*Fig.* 333 A), whereas in the complete one the cleft is V-shaped and tapers to a point (*Fig.* 333 B).

A B

Fig. 333.—A, 'U' shape of partial cleft palate (Veau Type II); B, 'V' shape of complete unilateral cleft of palate and lip (Veau Type III).

Maldevelopment of the mandible with regression is often associated with partial cleft palate, and on some occasions this gives rise to 'tongue-swallowing' soon after birth. When the baby lies on his back, breathing becomes stertorous and attacks of asphyxia may occur. When put to sleep at night, therefore, the child must not be allowed to lie on its back, but should be kept on its side for the first three months of life, by careful arrangement of sandbags in the cot: one is placed behind the back, and another behind the buttocks. Operation to hold the tongue

Table III.—Sex Distribution amongst Cases of Hare-lip alone, Cleft Palate with Hare-lip, and Isolated Cleft Palate

	Fogh-Andersen (1942) (625 Cases)				Present Series (1041 Cases)			
	Male		*Female*		*Male*		*Female*	
	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage	No. of Cases	Percentage
Hare-lip	90	65	48	35	139	60	94	40
Hare-lip and cleft palate	257	71	103	29	313	70	137	30
Cleft palate	43	34	84	66	144	40	214	60

forward is unnecessary, if the mother understands what is required and can be relied upon to do it.

Classification of the Types of Cleft in the Lip and Palate.—Hare-lip may be complete or incomplete, unilateral or bilateral.

Veau's classification of clefts in the palate is simple and the most useful:—

Type 1—Soft palate cleft.

Type 2—Hard and soft palate cleft.

Type 3—Alveolus cleft on one side as well as hard and soft palate.

Type 4—Alveolus cleft on both sides as well as hard and soft palate.

The last two are often associated with unilateral or bilateral hare-lip.

I. THEORIES ON CAUSATION

The cause of hare-lip and cleft palate is not known, but various factors are known to have an important bearing upon it. If the cause could be found, the incidence of congenital defects like this might be greatly reduced, or even prevented.

Two factors of proven significance have emerged: (1) Inheritance; (2) Unfavourable maternal environment during the 'critical period' of the first twelve weeks of gestation until the palate of the embryo has fused.

1. Inheritance.—A family history of the deformity was revealed in 12½ per cent of our 1041 patients. The mother's side of the family was affected nearly twice as often as the father's, but paternal predominance may occur, and is illustrated by an observation of Murphy (1947), who had as patients two children, one with right-sided hare-lip and the other with cleft palate. They had the same father, but different mothers.

Cleft lip and palate occur occasionally in uniovular twins (Lévy, 1928), but the cleft may be of a slightly different degree in each, which suggests that another factor besides the genetic one is involved. In our series cleft lip and palate was present in one twin (the other twin being normal) on 6 occasions, and in both twins on 1 occasion. Both fraternal twins may be affected (Shea and Nelson, 1947), but the difference in the type of cleft in each is usually more distinct.

Human somatic-cell nuclei contain 48 chromosomes arranged in pairs, one from each parent, and the genes on these are probably arranged in regular sequence and in a constant position. The ova and spermatozoa contain 24 chromosomes unpaired. The likelihood of two given recessive factors, which may cause a congenital deformity, meeting on the chromosome is increased eight-fold in first-cousin marriages. If congenital defects have already been noted in the family, the danger is even greater.

Fogh-Andersen (1942, 1946, 1948) found that 30–40 per cent of 703 patients with cleft lip or palate in Denmark had near-relations with similar deformities. He concluded that inheritance was the most important aetiological factor.

It seems likely that a recessive gene is responsible in most cases, but not all the babies who inherit the requisite genetic constitution suffer from the deformity. It is probable that the double dose of recessive factor makes the developing embryo unduly sensitive, especially during the 'critical period' of the first three months of gestation, to what would otherwise be unimportant variations in uterine environment. From the figures of incidence of the deformity in affected families, only one-quarter to one-half of those bearing the double dose of recessive factor develop the deformity. It seems likely, therefore, that additional influences exert their effect before the deformity becomes manifest. In short, there is a "genetic inclination and environmental provocation" (Crew, 1947).

'*Theory of Organizers*'.—Some additional influences which have to exert their effect before the deformity becomes manifest may also be genetic; and sex-genes or relative-growth-rate genes may also be involved. The 'theory of organizers' may be a correct interpretation of the course of events leading to normal development of the fœtus. It has been suggested that each developing tissue in the embryo 'organizes' the adjacent undifferentiated tissue into new tissues and organs, each link in development depending upon the completion of the previous link. This can be interrupted by a gene or by harmful agents such as viruses, radiation, or nutritional defects.

2. Unfavourable Maternal Environment.—Some of the maternal factors which produce an unfavourable environment and which might prevent proper fusion of segments in the embryo are:—

a. Malnutrition.
b. Vitamin A in excess or deficiency.
c. Cortisone therapy.
d. Insulin injections.
e. Rubella, and possibly other virus infections, such as mumps.
f. Toxæmia of pregnancy.
g. Pernicious vomiting of pregnancy.
h. Anoxia.
i. Radiation.
j. Rhesus sensitization.
k. Desoxyribonucleic acid ('D.N.A.') in excess or deficiency—a specific chemical substance with special genetic properties.

a. Malnutrition of the Mother during the First Three Months of Pregnancy.—Animal experiments suggest that lack of sufficient food or improper feeding during the first three months of pregnancy may uncover a pair of recessive genes or a gene which is but 'relatively dominant', and either of these may carry cleft-causing factors. Dr. Strauss (1914) studied congenital abnormalities in the animals of the Berlin Zoo, and reported that, previous to 1909, 32 jaguar cubs had been born with cleft palates. At that time all the jaguars were fed on cold meat from which the blood had been allowed to escape. The diet was changed; the parent animals were fed on meat which was still warm and which contained blood. Since then, on average, two litters a year have been reared, and no more cubs with cleft palates have been born. In the Dublin Zoo, where lions are successfully reared in captivity, cleft palate has been almost eliminated since the lionesses have been fed on fresh warm donkey meat. Some years ago, bulldog puppies, as well as many other kinds of puppy, were often born with cleft palates, but since the necessity for giving fresh meat to all pregnant bitches has been recognized, the incidence of cleft palate has fallen remarkably.

In the good old days, before rationing and before the post-war 'improvement of living conditions', it was well recognized that hare-lip and cleft palate occurred more frequently in the children of poor people than in the families of the well-to-do. Now this difference has fortunately disappeared, but congenital abnormalities of all kinds, including cleft lip and palate, are thought to be more common in 'unwanted children' and those born out of wedlock or, as the Irish would say, of 'illegitimate parents'. If this is true, it might be caused by malnutrition of the mother; because fright and worry lead to loss of sleep and appetite and to poor digestion; this leads to malnutrition. Murphy (1947), however, investigated nearly 2000 babies in Philadelphia, of which 759 were born out of wedlock, and observed that malformation affected illegitimate offspring no more often than those born in wedlock (each 1·1 per cent). Only 6 of our 1041 deformed patients were known to have been born out of wedlock (0·6 per cent).

b. Vitamin A in Excess or Deficiency.—In the rat, massive overdoses of vitamin A to the dam during early and middle pregnancy result in cleft palate in the offspring (Cohlan, 1953; Giroud and Martinet, 1954); whereas Warkany (1947) produced hare-lip and cleft palate in the rat by deprivation of vitamin A, as well as by deprivation of riboflavin.

c. Cortisone.—Recently in Cambridge, Woollam and Millen (1957) showed that if cortisone was given to pregnant rats simultaneously with overdoses of vitamin A, the incidence of cleft palate in the offspring was greatly increased, and nearly all the offspring developed it. Cortisone seems to increase the sensitivity of developing tissue and helps to prevent normal segmental fusion. Fainstat (1954) also showed that if cortisone was given to pregnant rabbits and rats, cleft palate was common in the offspring.

If cortisone is given to a pregnant woman early in her pregnancy, i.e., before the twelfth week when the palate has normally fused, there is a great danger of cleft palate occurring in her baby. In 1955 Higuera Rojas and Lardelli made a case report of a woman with Cushing's syndrome who gave birth to a baby boy with isolated cleft palate with associated mandibular regression: attacks of tongue swallowing and asphyxia occurred when the baby lay on its back. In 1956 Harris and Ross, and Doig and Coltman, described the occurrence of cleft palate in babies whose mothers had been given cortisone in the early weeks of their pregnancies. Wells's (1953) figures suggest that cortisone administration in early pregnancy may increase the chance of congenital abnormality in the baby. Twenty-seven mothers received cortisone, and three of their babies were born with congenital deformities, other than cleft lip and palate.

d. Insulin.—Duraiswani (1950, 1952) produced genetic defects by timed injections of insulin into incubating eggs. The site of the abnormality varied with the time of injection. A single injection during the first 48 hours after the start of incubation was likely to produce a defect in the vertebræ, whereas on the third day only the feet were affected. Furthermore, some of these induced defects were subsequently passed on to the next four generations, which suggests that an unfavourable environmental factor may induce a mutation which may then be transmitted to future generations.

In human beings, Wickes (1954) has mentioned the possible danger of giving large doses of insulin to a pregnant woman before the tenth week of gestation. He described a case in which a schizophrenic mother, given a course of insulin injections to induce coma, gave birth to an infant with hypertelorism and optic atrophy. At that time, in the early weeks of pregnancy, she was not known to be pregnant.

Moreover, the death-rate (56 per cent) and the incidence of congenital deformities (8·6 per cent), in babies born to diabetic mothers, are well known to be high. (Oakley, 1953; Gilbert and Dunlop, 1949.)

e. Rubella and Other Virus Diseases.—In certain bacteria, e.g., *Salmonellæ* and *B. coli*, it has been shown that a virus can act as a genetic agent (Hayes, 1958). By a process called 'transduction', an active particle of desoxyribonucleic acid can be conveyed to the nucleus of the host by an infecting virus. Under the electron-microscope the spiked tail of the virus can be seen to pierce first one nucleus, then another. A small nuclear particle, composed of desoxyribonucleic acid, may remain on the infecting spike of the virus after piercing the first nucleus, and when this is withdrawn on the spike, it may be left inside the nucleus of the next bacterium, which it attacks. Thus, a specific genetic substance is conveyed from one host nucleus to another.

It seems probable that in the human mother a virus may pass through the placental barrier, like an Rh antigen, and may damage the embryo or alter its development at the 'critical period', which is during the first three to four months of gestation, when the tissues are in process of development into organs and are extremely vulnerable. After this time, the tissues have been differentiated to form organs, and proceed merely to increase in size; after the fourth month the direction of development is firmly established and the fœtus is therefore less vulnerable.

Grönvall and Selander (1948) found the frequency of virus disease contracted in the early months of pregnancy ten times greater in the mothers of deformed children than in a control group who were mothers of normal babies.

i. *Rubella*: In 1941 Gregg found that many babies who had congenital eye, heart, and ear defects had been born to mothers who had suffered from a severe form of rubella during the first four months of their pregnancies.

The exact risk to the child is still not known. Swan (1944), in a retrospective analysis of 117 deformed babies, considered the risk almost 100 per cent if rubella was contracted during the first two months of pregnancy. This is now considered a fallacious method of analysis. Prospective methods of analysis are now being carried out upon women actually observed to develop rubella during the first four months of pregnancy. The incidence so far in a small number of patients followed through to term is much less, and the estimated risk to the child is probably between 10 and 25 per cent (Fox and Bortin, 1946; Brown and Nathan, 1954; Greenberg, Pellitteri, and Barton, 1957; Pitt, 1957). Rubella contracted by a pregnant woman after the fourth month of gestation does not seem to cause any serious risk to the child.

The exact time in the pregnancy at which the disease is contracted determines fairly accurately the type of deformity which results (Gregg, 1944). If contracted in the 4th to the 9th week, the heart is affected; from the 5th to the 8th week, the eye is affected; and between the 7th and the 12th week, the ear is affected.

Lundström (1952, 1953) observed that although a mother had previously contracted rubella in childhood and was apparently immune, this did not give her child complete protection. He observed that when immune mothers were in contact with rubella early in pregnancy, for instance when other members of the family developed the disease, the frequency of congenital abnormalities in their babies was 12 per cent, a figure significantly higher than that found in babies born to mothers who had not been in contact with rubella during early pregnancy.

McDonald (1957) made a partially prospective study of 3300 women in pregnancy; 122 congenital defects were observed amongst their babies. Rubella occurred only 3 times amongst the mothers of these 122 abnormal babies, and each time a patent ductus arteriosus was the defect noted.

Nowadays it is a common practice to avoid isolation when an epidemic of rubella occurs at a girls' school. As between 0·3 and 0·4 per cent of patients with rubella are said to develop encephalitis (Cantwell, 1957) it is doubtful whether therapeutic infection of young schoolgirls is justifiable. Although rubella encephalitis is usually self-limiting and not followed by a permanent nerve lesion, there is a mortality from it of about 21 per cent.* (Schleisner, Thorsteinsson, and Bøgèskov-Jensen, 1955; Jørgensen, 1955.)

In our series, 500 patients were investigated in retrospect; a history of rubella or rubella contact in the mother during the first four months of pregnancy was obtained on 5 occasions only (1 per cent). I think, nevertheless, it is of vital importance that children who contract rubella at school should avoid all contact with their mother when she happens to be in early pregnancy, or anyone else in a similar condition.

ii. *Mumps*: Swan (1944) described the effects of mumps upon 3 pregnant mothers. Two contracted the disease late in pregnancy and their babies suffered no ill effects. One contracted the disease early in pregnancy and her baby suffered from a congenital corneal lesion. Grönvall and Selander (1948) described 38 mothers who suffered from mumps during their pregnancies. Five malformed babies were born, and there was 1 abortion. Murphy (1947) stated that congenital deformities had been reported in the babies of mothers who suffered not only from mumps, but also from chicken-pox, in early pregnancy.

f. Toxæmia of Pregnancy.—Murphy (1947) reported the presence of some sign of kidney disease or hypertension (blood-pressure over 130 mm.) during pregnancy of 30 per cent of 453 mothers of malformed children. A history of toxæmia in the mother's pregnancy was obtained in only 4 of 500 of our patients investigated for this (i.e., 0·8 per cent).

g. Pernicious Vomiting of Pregnancy.—This occurs especially during the first three months of pregnancy, at a time when the embryo is most sensitive to any adverse conditions of nutrition, and it may be a factor in the causation of congenital defects, but it was noted only once in our series.

h. Anoxia, Anæmia, and Threatened Abortion.—Ingalls and his co-workers (Ingalls and Gordon, 1947; Ingalls, Curley, and Prindle, 1950) caused congenital defects in mice by anoxia of the mother. The type of deformity induced depended upon the period in gestation at which the anoxia was applied, and the organs affected were those in most active development at that stage. The degree, also, of anoxia affected the outcome, and they noticed that if a pregnant mouse was submitted to anoxia on the eighth day, the head of the fœtus was malformed. If the anoxia was severe, anencephaly resulted; if mild, cleft palate occurred. They inferred that any noxious agent can produce any type of congenital deformity if applied at the appropriate stage of gestation. They suggested that in human mothers, not only grave anoxia, but also the relative anoxia associated with anæmia or with mild stagnation of circulation, or with threatened abortion, may be factors predisposing to congenital malformation of their offspring.

Murphy (1947) found that anæmia was present in mothers who gave birth to malformed children more often than in mothers who gave birth to normal children. McDonald (1957), in his study of 3300 women in pregnancy and the 122 congenital defects in their babies, observed that anæmia (Hb under 80 per cent) was more frequent among mothers giving birth later to abnormal children than mothers of normal infants. In our 500 patients a history of threatened abortion during the pregnancy was noted on 2 occasions (0·4 per cent). Nevertheless, it may be that high-altitude flying without adequate precautions against anoxia should be avoided in the first four months of pregnancy.

i. Radiation.—In animals, exposure of the mother to X rays was found to cause congenital deformities in the offspring (Russell and Russell, 1954), and Warkany (1947) quotes an incidence of abnormality, after exposure of 144 mother rats to X rays early in their pregnancy, of 485 out of 622 offspring, i.e., 78·6 per cent.

Most animal experiments have shown that the majority of mutations, which occur naturally or following artificial radiation, are at least partially recessive and so may not be detected in the first generation after exposure.

It is probable that the cosmic rays of the atmosphere may induce natural mutations in Man. Murphy (1929) reported the effects of radiotherapy upon 106 women, and found that one-third of their offspring, who were born alive, were severely deformed. It is possible that exposure of pregnant women to X rays may provoke congenital abnormalities, especially if a genetic inclination is already present. X-ray examination of a pregnant woman's pelvis, as well as virus infections or threatened abortion, may lead to leukæmia in her infant (Stewart, Webb, Giles, and Hewitt, 1956; Stewart, 1957; and Stewart, Webb, and Hewitt, 1958). It may also, I think, provoke congenital abnormalities.

* Schleisner, P., Thorsteinsson, J., and Bøgèskov-Jensen, I. (1955), reviewed 75 cases of rubella encephalitis and reported 16 deaths.

The dose of irradiation received by the fœtal gonads during diagnostic pelvimetry frequently exceeds 2·5 r (Osborn and Smith, 1956). Therefore X-ray examination of the hips, abdomen, and pelvis (which is included in most urinary tract examinations) of mothers early in pregnancy should probably be avoided. X-ray investigations should only be done if the mother's life might be in danger without them. Possibly, radiation of a father's testes may predispose to congenital abnormality in his baby. There is also a possibility that pregnant women living near atomic piles may suffer this danger. Despite repeated official denial, an example of dangerous diffusion of radio-activity has occurred recently at Windscale, where the experts had assured the local population that the risks were negligible.

Mongols result from a special type of mutation, and they tend to occur in the babies of older women. This might be explained by the fact that older women have lived long enough to have received enough exposure to small doses of natural cosmic radiation or artificial irradiation for this to be effective. We have not found cleft lip or palate to be more common in later pregnancies or in the offspring of older mothers, though Malpas (1937) did, and Murphy (1947) found that congenital malformations occurred least frequently in the babies of mothers between 20–25 and increased in frequency after 30 years, and was greatest over 40 years. Also a prolonged period of sterility often preceded the birth of a malformed child, but we have observed this only twice.

j. Rhesus Sensitization.—Rh sensitization may be another adverse factor which helps to provoke the onset of congenital abnormalities. When a Rh-negative woman is married to a man who is Rh-positive, the first baby's antibodies may sensitize its mother; so that in later pregnancies iso-agglutination may develop and the maternal antibodies may pass through the placenta to her next unborn baby. Levine (1942), Penrose (1946 a, b), and Weiner (1947) noted that hare-lip and cleft palate and other congenital deformities seem to occur when Rh iso-sensitization is present in the mother more often than when it is absent. Weiner investigated the blood of parents of 19 babies born with congenital abnormalities in which the mothers' blood contained iso-agglutinins, and found cleft lip and palate in 2 of the 19 babies. He suggested that the antigen-antibody reaction in the fœtus results in the blocking of terminal vessels by intravenous clumping of red cells, as well as intravascular hæmolysis. When this occurs in certain regions, near points of normal fusion, closure may be prevented, and hare-lip, cleft palate, or other fusion defects, like spina bifida, may result. This Rh-sensitization factor has not been proven, but it is worthy of further study. No information has been obtained about Rh sensitization of the mothers of our cleft lip and palate babies, but the incidence of first-born amongst our patients was almost as high (40 per cent) as in all other babies first-born in England, Wales, and Scotland in 1956 (42 per cent), and Rh sensitization can certainly be excluded from these (*Table IV*).

Table IV.—Position in Family of 643 Cleft Lip and Palate Patients compared with All the Children born during 1956 in England, Scotland, and Wales

	Order of Birth	1st-born	2nd-born	3rd-born	4th-born	5th-born	6th-born	7th-born	8th and Subsequent Births	Total
Cleft Lip and Palate	No. of patients	273	174	92	48	27	17	15	7	643
	Percentage (approx.)	42	27·5	14	7	4	2·5	2	1	100
Control	No. of all children born in England, Scotland, and Wales during 1956	296,713	220,664	113,060	55,429	28,268	14,521	7,993	9,665	746,313
	Percentage (approx.)	40	30	15	7	4	2	1	1	100

k. Desoxyribonucleic Acid ('*D.N.A.*').—Nucleic acids have been shown to possess biological and genetic specificity, the exact chemical nature of which has not yet been determined. Desoxyribonucleic acid has been shown, however, to be the fundamental substance of which genes and chromosomes are made. It can also be the fundamental transposing agent in the production of mutation and in alteration of type. It may, therefore, be involved in the cause of congenital abnormalities resulting from mutation. Desoxyribonucleic acid has a big molecule capable of existing in a myriad of different forms, each subtly different from the others in its internal chemical architecture. It is possible that different hereditary qualities are carried in different and chemically specific forms of desoxyribonucleic acid. Experiments on bacteria (Avery, MacLeod, and McCarthy, 1944; Dawson and Sia, 1931; and Sia and Dawson, 1931) have proved that by injection of 'D.N.A.' into the growth media of type-specific *S. pneumococci*, it is possible to change the type of pneumococcus. Moreover, the chemically induced alterations in cellular structure and function are predictable, type-specific, and genetically transmissible. Division of certain bacteria is often preceded by fusion—surely the most primitive type of copulation—whereby the nuclei of two bacteria fuse before division. The degree of fusion can be controlled and interrupted by careful timing (Hayes, 1958; Wollman, Jacob, and Hayes, 1956). The fusion takes place in a regular manner and certain parts of the nuclei, containing certain genes, fuse first, and the rest of the nuclei and their genes proceed to fuse in a regular and orderly sequence afterwards. Interruption of fusion at a certain specific time will result in the transmission of certain specific portions of the nucleus and its chromosome and genes. It is possible to control, by this method of timing, the transmission of

certain genes and the hereditary factors in them. A fundamental experiment in heredity has been achieved in bacteria, in which the nuclei are simple, and probably contain only one chromosome. Moreover, the simple bacterial nucleus is haploid, i.e., the somatic nucleus contains only one representative chromosome or gene, instead of bearing paired chromosomes and genes as in the vertebrate somatic nucleus, which contains one gene or chromosome plumage, and figure, resembling the Khaki-Campbell. Moreover, some of these characters were transmitted to the next generation. If this is a true example of inheritance of acquired characteristics, the characters have been acquired by injection of a specific genetic substance whose chemical constitution is known—desoxyribonucleic acid. If these findings are substantiated by controlled and more scientific experiments, a great advance will have been made. It

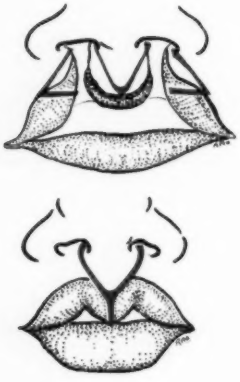

FIG. 334.—Repair of complete (and almost complete) unilateral hare-lip and nostril deformity (Le Mesurier's operation).

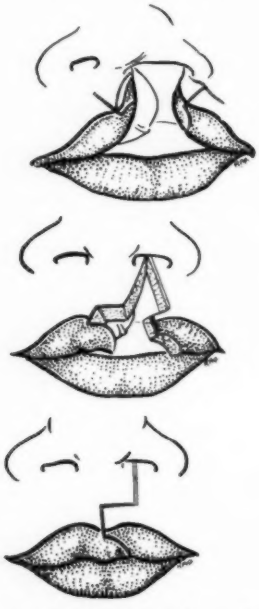

FIG. 335.—Repair of minor degree of hare-lip without nostril deformity (Kilner's operation).

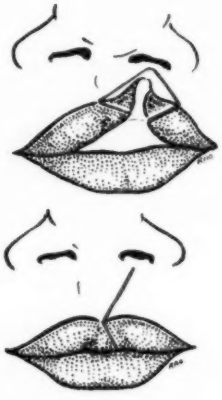

FIG. 336.—Repair of bilateral hare-lip.

from each parent. Whether this experiment can be repeated in higher organisms with more elaborate cell nuclei remains to be seen. Nevertheless, the experiment gives a clear insight into the construction of the nucleus in its simplified form, the regular arrangement on the chromosome of the genes contained on it, and the chemical specificity of the nucleic acids of the desoxyribonucleic acid series, in the transmission of hereditary factors.

In vertebrates, the only published experiments in the use of 'D.N.A.' injections for the production of gene modifications and transmission of hereditary factors by specific chemical means have come from France (Professor Benoit, Father Leroy, and Mme. and M. Vendrely, 1957 a, b). The now celebrated 'French ducks' have caused a stir in the world of genetics, but the experiments were not scientifically controlled and are at present only suggestive and unproven. The French workers prepared 'D.N.A.' from the testes and nucleated red blood-cells of Khaki-Campbell drakes and injected this into Pekin ducklings, when they were about eight days old. A significant proportion of them grew up into ducks which had certain characteristics, such as beak colour, suggests that the chromosomes, instead of forming always an exact replica of themselves as they grow before division, are able to assimilate foreign and slightly different forms of nucleic acid: but it is difficult to see how 'D.N.A.' injected into the ducklings after hatching could alter genetic type so late. It seems possible also that the strains of ducks used for the experiment were not genetically pure. It is also possible that the French ducks themselves may have lacked an inherent purity and failed to discourage the clandestine and flying visits of a mallard drake.

II. TREATMENT

1. HARE-LIP

The object of treatment is to improve the appearance of the lip and nostril and to provide a short lip which curves forwards and rolls outwards at the lower margin, *with minimum risk to life.*

Time for Operation and Preparation.—The time to repair the nostril and lip is when the baby is thriving and weighs 12 lb. or over. The mother is admitted with her baby so that she can look after

it and act as a special nurse. Cultures are taken from the nose and throat before operation so that suitable antibiotic cover can be provided: the operation is postponed if a virulent organism such as a bate

FIG. 337.—Incorrect repair of bilateral hare-lip. Colour photograph showing that the red mucosa of the prolabium has been inserted in error into the free margin of the vermilion border.

FIG. 338.—After adjustment. Colour photograph taken on the day after the stitches were removed.

FIG. 339.—Colour photographs of complete unilateral hare-lip before and after operation.

hæmolytic streptococcus or a penicillin-resistant staphylococcus is found. The hæmoglobin is estimated, because the presence of even a moderate degree of anæmia means that the operation should be delayed and intramuscular 'Imferon' injections started. An X-ray examination of the chest is done as a routine procedure before operation to exclude other congenital abnormalities in the heart or lungs.

Anæsthetic.—An intratracheal tube should always be used to administer an anæsthetic to a baby for a major operation. Gas, oxygen, and ether on open circuit (Ayre, 1937) is the safest method. Safety also depends on the child waking up immediately after the intratracheal tube is removed. The anæsthetic should therefore be very light, so that when the tube is removed at the end of the operation the child cries and expands its lungs.

After-treatment.—Denis Browne's hare-lip bow is used after operation to prevent tension on the stitches, and so that they can be removed on the third day, thus avoiding stitch-marks.

OPERATIONS FOR HARE-LIP

1. Unilateral.—

a. Complete (and the severe type of incomplete, if the nostril deformity is pronounced).—Le Mesurier's method (1952, 1955): A rectangular flap is made on the outer side of the cleft. It is rotated through almost a right angle, to provide full width at the vermilion border. By this method a much better nostril, as well as lip, can be made. (*Fig.* 334.)

In some severe degrees of incomplete hare-lip, when the nostril and lip deformity is pronounced, it is wise to make the cleft in the lip complete, and to treat it as a complete one.

2. Bilateral.—A bilateral hare-lip can be repaired in one stage. If the premaxilla is tilted forward, a small triangle of bone is removed from the junction of the premaxilla and prolabium to mobilize the central portion (Berry and Legg, 1912). It is important when suturing to unite the junction of the vermilion and pink skin on each lateral element to a point a little distance lateral to the mid-point of the U which is made on the central prolabial skin (Denis Browne, 1949). (*Fig.* 336.)

No prolabial 'vermilion' is ever allowed to appear on the free border of the lip, but the red mucosa on the prolabium is freed and allowed to slide backwards and is used to form the lining of the undersurface of the central part of the lip (*Figs.* 337, 338).

FIG. 340.—Colour photographs of hare-lip patients of different ages after repair.

b. Incomplete.—In the minor degrees, without nostril deformity, simple excision by Kilner's (1928) modification of Rose's (1868, 1874, 1879) method is all that is required (*Fig.* 335). Complicated flap operations are unnecessary.

Results.—

Deaths.—Amongst 530 consecutive patients operated upon by me for repair of hare-lip deformities, 4 patients have died in hospital after operation, an operative mortality of 0·75 per cent.

Anatomical Results.—No attempt has been made to classify anatomical results (*Figs.* 339, 340), as no accurate scientific criterion of this seems possible.

The complete unilateral hare-lip with severe nostril deformity is the most difficult type to treat. My results have improved, I think, since Dr. Le Mesurier came to stay with me for a few days in 1953. He very kindly showed me how to do his operation and I now use his method for these patients, and believe that the nostrils are more symmetrical and the lips shorter and pout more at the vermilion border than after the earlier methods I used.

In the minor cleft, however, I think it is unnecessary to do an elaborate flap operation, and still use the straight excision method (Rose) which was perfected by Kilner, and obtain better results for these patients than by a flap operation.

In general, it may be said that the parents are nearly always delighted, but the surgeon is rarely satisfied. The mother graciously compares the result with the condition of the baby before operation, whereas the surgeon should compare the result with a normal child. The lip should be comparatively short and well rolled outward at the vermilion border where the Cupid's bow is well-marked and pouting. The nostrils should be symmetrical and the nose straight, with the columella centrally placed and of natural length.

Much improvement can often be made by a minor 'trimming' operation when the child is 5 or 6 years old, if scars or asymmetry are visible at this time.

2. CLEFT PALATE

The principal aim in treatment should be to provide an adequate speech mechanism which is ready to function at the time when the child first learns to speak. Palate repair should therefore be complete before the child is 2 years of age. There seems no object in doing the operation before the child is 1½ years old.

When considering any operation, it is essential that the risk to life should be the prime consideration, but this is sometimes forgotten. Results of operation for repair of the palate in patients under one year old reveal a forbidding mortality of 10 per cent or over. In the children who are operated on between 1½ and 2 years the mortality should be below 1 per cent. Although in the complete cleft the upper alveolus may be irregular afterwards, and sometimes contracted, adequate orthodontic treatment by an expert can usually deal with this, and the disability arising from this is insignificant in comparison with the advantage of normal speech. When the patient is looking for a job in later life, speech is of much greater importance than the position of his upper teeth.

An intratracheal tube is essential for safety. To prevent compression of the tube between the lower incisor teeth and the tongue-piece of the Kilner's Shadwell gag, a special long metal connector is essential. A grooved tongue-piece (Russell Davies, 1954) is a useful refinement and helps to avoid kinking of the intratracheal tube. Continuous suction by two catheters inserted through the nostrils into the nasopharynx is an added precaution and is a great help during the operation. A hand suction tube, controlled by the assistant, is essential and, if used by an experienced assistant, swabs need not be used. If, however, the assistant does not understand the details of the operation, small swabs may be required. Periodically, the mouth should be cleared of clots by irrigation, using a rubber bulb syringe.

Technique of Operation.—The standard operation described by Wardill (1937) and Kilner (1937), which is a modification of the principles expounded by Veau (1931), will yield standard and reasonably good results if the surgeon is careful. Interference with the pharyngeal muscles by any form of pharyngoplasty seems to me to be unwise in a primary case. No large series of cases has been reported which would support the theory that these operations improve results in cleft palate repair. Many types of muscle transplant have been described since the time when Botey (1907) described the first pharyngoplasty and Rosenthal (1924) described his pharyngeal flap operations. After trial, each in turn has fallen into disrepute, and I think that all the modern modifications of these will suffer the same fate as did the Wardill pharyngoplasty. When a muscle belly is transplanted it does not contract actively afterwards unless transplanted with its own motor nerve intact. Muscle transplants, unless specially designed with this in view,* form fibrous bars of scar tissue, and this is what happens to most transplants containing pharyngeal muscle.

The first and most important phase in the operation for repair of the palate is to free the soft tissues widely from the cleft bone and then to unite the separated muscles and mucosa in the middle line. The floor of the nose should always be closed by suturing the nasal mucosa; then the muscles of the soft palate are united in the midline to complete the levator sling, which is the most important muscle used for nasopharyngeal closure. Finally, the buccal mucosa is repaired. The length of the soft palate is of less importance than its muscularity and mobility. A thick, muscular soft palate which is mobile and in which there is a strongly arching levator sling is much more useful than a long flabby one.

It is essential to avoid damage to the posterior palatine arteries, because an adequate blood-supply to the soft palate depends on these arteries. The posterior palatine arteries, if carefully freed from the surrounding soft tissues and the margins of the posterior palatine foramina, never prevent the two sides of the palate from being brought to the middle line without tension. (Oldfield, 1941, 1947, 1949.)

As in hare-lip operations, safety depends very much upon the anæsthetic being light during the later stages, so that the patient can cough and cry as soon as the tube is withdrawn.

After-treatment.—The tongue is held forward by a stitch through the dorsum of the tongue attached by adhesive tape to the centre of the chin. This stitch prevents the asphyxia which is caused by falling backwards of the tongue during the first night. The patient is kept lying on his side and tap-water is given by rectal drip. Glucose water is also given by a spoon as soon as the child is awake after the anæsthetic.

* E.g., Clark's operation (1946) for replacement of the biceps brachii by the outer part of the pectoralis major with the outer branch of the lateral anterior thoracic nerve alongside it.

After the first 48 hours soft solids are given, and a drink of water at the end of each feed is used as a mouth-wash. It is best to avoid milk, because this clots on the stitches and tends to make the mouth foul. As chromic catgut is used for all the stitches, no palate stitch requires removal. It is important to avoid any form of local treatment to the palate, and it is advisable not even to look in the mouth until after the tenth day. If all is well then, the child goes home between the tenth and fourteenth day. Arrangements are made for a course of speech training and blowing exercises to start one month after leaving hospital, and this is continued until speech is as near normal as possible.

Table V.—Speech Results in 397 Cases of Cleft Palate reviewed after Operation

Excellent		Fair		Bad	
No. of Cases	Percentage (approx.)	No. of Cases	Percentage (approx.)	No. of Cases	Percentage (approx.)
303	77	71	17	23	6

Fifteen per cent of our cleft palate patients required treatment from an ear, nose, and throat surgeon, because the tendency to middle ear infection and deafness is not prevented by repair of the palate. Many patients require careful supervision if deafness is to be prevented. Tonsil dissection may be required, but removal of the adenoids should be avoided unless the patient is likely to go deaf without it.

Results.—An analysis has been made of 710 consecutive cleft palate patients upon whom I have operated. Of these, 648 were 'primary' and 62 were 'secondary', the latter having had previous unsuccessful operations elsewhere.

Deaths.—There have been 7 deaths following operation for repair of the palate in the 710 patients—a mortality of just under 1 per cent.

Speech Results (*Table V*).—In the examination of 397 patients who have been reviewed for speech results, the patients were asked to articulate the consonant sounds which may cause difficulty when the palate has been cleft. The results have been tabulated on a chess-board type of record card. Following conversation with the patient, nasal tone, huskiness of the voice, and the general clarity of articulation were recorded in separate columns. The cases were classified into three groups:—

Group I. Excellent: Patients with natural speech who could pronounce all consonant sounds correctly. (303 cases.)

Group II. Fair: Patients who could speak so clearly that strangers could easily understand them. Often, however, when excited or talking fast, their intonation was 'nasal' or 'husky'. In some, one or other of the sibilant sounds, although pronounced, was imperfect. (71 cases.)

Group III. Bad: Patients whose speech had the typical cleft palate characteristics and who were difficult for strangers to understand. (23 cases.)

Favourable speech results were found in 77 per cent, fair results in 17 per cent, and bad results in 6 per cent.

Anatomical Results (*Table VI*).—The anatomical result was reviewed in 494 of the patients whose palates I had repaired. In comparison with speech, these results seem to be of minor importance, and may be summarized briefly into four groups:—

Table VI.—Anatomical Results in 494 Patients reviewed after Operation for Repair of the Palate

	Group I: Closure Complete. Soft Palate mobile and arching well		Group II: Closure of Soft Palate only by Gillies-Fry Procedure		Group III: Closure Incomplete. Hole in Hard Palate, but Soft Palate mobile and arching well		Group IV: Soft Palate Stiff, does not arch		No. of Patients
	Nasopharyngeal Valve Competent		*Nasopharyngeal Valve Competent*		*Nasopharyngeal Valve Competent*		*Incompetent Nasopharyngeal Valve*		
	No. of Patients	Per-centage	No. of Patients	Per-centage	No. of Patients	Per-centage	No. of Patients	Per-centage	
Cleft palate associated with hare-lip	206	82·7	6	2·5	22	8·8	15	6·0	249
Cleft palate only	221	90·2	1	0·4	11	4·5	12	4·9	245
Total	427	86·4	7	1·4	33	6·6	27	5·6	494

Group I: Hard and soft palate repair complete, the soft palate being muscular, mobile, and arching well, and the nasopharyngeal valve competent. (427 cases—86·4 per cent.)

Group II: Soft palate repaired by Gillies-Fry procedure, with obturator in hard palate defect, and nasopharyngeal valve competent. (7 secondary cases—1·4 per cent.)

Group III: Closure of hard palate incomplete, a small hole being present in the anterior third of the hard palate. The soft palate was mobile and arched well, and the nasopharyngeal valve competent. (33 cases—6·6 per cent.)

Group IV: Soft palate stiff, not moving adequately, and not arching enough to close the nasopharyngeal isthmus; nasopharyngeal valve therefore incompetent. (27 cases—5·6 per cent.)

Favourable anatomical results were found in 94·4 per cent and bad results in 5·6 per cent.

SUMMARY

A short review is given of 1041 cases of hare-lip and cleft palate treated by one surgeon. Some ideas

on the possible cause of this type of congenital abnormality are given. The methods of treatment and the results of treatment are described briefly.

The lip should be repaired only when the baby is thriving and after attaining the weight of, say, 12 lb. The Le Mesurier rectangular flap method was used for a complete unilateral hare-lip with severe nostril deformity, but a simple straight excision technique (Kilner) was used for minor unilateral and for bilateral hare-lip cases.

Satisfactory results can be obtained by the well-tried method of Wardill and Kilner for repair of the palate. The posterior palatine arteries should never be divided. The nasal mucosa above the hard and soft palate should be closed by catgut sutures, as well as the muscles of the soft palate and buccal mucosa. It is more important to provide a strong arching soft palate than a long flaccid one. Length is not as important as muscularity and mobility. Operations involving incisions in the posterior pharyngeal wall and muscle transplants should be avoided in all primary cases. The ideal age for repair of the palate is between 1½ and 2 years.

In the future, efforts should be made, not only to improve treatment, but also to *prevent* hare-lip and cleft palate. The time has now come when extensive research should be undertaken to investigate the cause of congenital deformities so that their incidence could be reduced, and so that some day they may be prevented. It is not enough just to wait and treat them after they have occurred.

I am grateful to my two anæsthetists, Dr. F. Mackintosh and Dr. H. Harris, whose patience and skill made this work possible. I am indebted to Professor T. Pomfret Kilner and Dr. W. Goldie for much kind advice, and to my wife Rosamund for the drawings.

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ANGIOSARCOMA IN POST-MASTECTOMY LYMPHŒDEMA

A REPORT OF 5 CASES AND A REVIEW OF THE LITERATURE

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THE development of a highly malignant lymphangiosarcoma as a complication of long-standing post-mastectomy lymphœdema in the upper extremity was first described by Stewart and Treves in 1948 when they published details of 6 cases. Since this time 17 further cases have been recorded by various authors (*see Table I*).

The clinical details of the 23 cases so far recorded are essentially similar. The patients give a history of carcinoma of the breast treated by radical mastectomy, with or without associated radiotherapy, and complicated a short time after the mastectomy by the development of a persistent lymphœdema of the ipsilateral arm. Following a cancer-free latent period of several years a new neoplastic lesion develops in the œdematous upper extremity.

The new lesion starts as a solitary, purplish-red, subdermal, slightly raised, macular or nodular lesion situated in the skin of the arm or antecubital area, and described by the patients as a 'bruise'. This is shortly followed by similar satellite tumours and once the process is initiated the nodules continue to grow, new ones appearing on the forearm, dorsum of the hand, and skin of the adjacent thorax. The individual growths are flattened on top, soft in consistency, and on section show a greyish-red, soft, central portion, with a purplish-red perimeter. Larger lesions become necrotic and cystic. The tumours remain aggressive and unless treated early and radically will soon cause the death of the patient from metastatic and residual growths.

The condition has received little attention in the British literature, only 2 cases having been recorded (Hall-Smith and Haber, 1954, and Kettle, 1957). However, it is important that the surgeons and radiotherapists responsible for the long-term follow-up of cases of carcinoma of the breast should be aware of the possibility of a sarcomatous change being superimposed on post-mastectomy lymphœdema of long duration. It is proposed in this paper to describe the clinical details of 5 patients, all of whom had had successful combined surgical and radiotherapeutic treatment for carcinoma of the breast and been left with varying degrees of post-mastectomy lymphœdema. Three of the cases are undoubted examples of the fully developed Stewart-Treves syndrome, and the other 2 cases appear to be the 'premalignant' phase.

CLINICAL FINDINGS

1. Fully Developed Examples of the Stewart-Treves Syndrome.—

Case 1.—Mrs. B. L., aged 41 years, was referred to hospital in December, 1943, complaining of a lump in her left breast. The lesion was clinically a scirrhous carcinoma and radical mastectomy was performed. Histological examination of the breast tumour showed an anaplastic scirrhous carcinoma. A course of post-operative radiotherapy was given in February, 1944. In May, 1944, lymphœdema of the left arm was noted; this was initially attributed to a recurrence of the malignant process in the axilla and was treated for a short time with stilbœstrol.

Apart from the persistent brawny œdema of the left arm, which extended from the shoulder to the hand, the patient remained well and free from any evidence of malignancy for just over ten years.

In March, 1954, she attended hospital with a large purplish swelling over the inner aspect of the upper part of the left arm which had been present for 5–6 weeks and was rapidly increasing in size.

On examination her general condition was fairly good and there was no evidence of any recurrent malignancy in the treated area of the left breast. The left arm showed brawny œdema from the shoulder to the hand and there was a large, reddish-purple, tender mass on the upper part of the arm, with similar smaller discrete purplish satellite nodules, both on the arm and the adjacent chest wall. Two of the nodules were excised, one from the arm and one from the chest wall; both showed the typical appearances described in the recorded cases of the Stewart-Treves syndrome.

The patient was treated palliatively and died in August, 1954, eight months after the first indication that all was not well with the œdematous arm. Unfortunately, a post-mortem examination was not obtained, but as dyspnœa had been a marked terminal feature it is probable that pulmonary metastases were present.

Case 2.—Mrs. G. E., aged 44 years, was referred to hospital in November, 1948, with a history of a lump in her left breast of four weeks' duration. On examination there was a large mass in her left breast with a mobile gland in the left axilla. A clinical diagnosis of carcinoma was made. She received a course of pre-operative radiotherapy and in February, 1949, a radical mastectomy was performed which was followed almost immediately by œdema of the left arm. Histological examination of the mastectomy specimen showed a degenerate carcinoma without involvement of lymph-nodes. In November, 1949, a small nodule was noted near the upper end of the scar and an enlarged possibly malignant gland in the right axilla; a course of testosterone was instituted but after seven months this was discontinued, the nodules and glands remaining unchanged.

Apart from the persistent œdema of the left arm the patient remained well and free from any malignancy for eight years. In October, 1956, she attended hospital with a bluish-purple swelling on the anterior aspect of the left upper arm of one to two months' duration.

On examination her general condition was good. There was no evidence of any recurrent malignancy at the site of the mastectomy. The left arm showed in addition to a moderate degree of brawny œdema of the whole arm (maximum circumference 30 cm.) extensive 'bruising' and induration of the anterior aspect of the upper arm. Arising from this 'bruised' area there was a purplish-red tumour about 2·5 cm. diameter; the central part was occupied by a dark purple-black elevated papule (0·8 cm. diameter), the surface of which was bleeding. Around this papule the skin was indurated, slightly elevated, and pinkish in colour (*Fig.* 341). A diagnosis of angiosarcoma or melanoma was made and the tumour excised. Histological examination confirmed the diagnosis of angiosarcoma complicating post-mastectomy lymphœdema and the arm was successfully amputated at the shoulder joint in November, 1956. In the short time between the first

Table I.—Cases of Lymphangiosarcoma recorded in the Literature since 1948

Author	Age at Radical Mastectomy	Side of Mastectomy	Associated Radiotherapy	Cancer-free Latent Period (Years)	Method of Treatment of Lymphangiosarcoma	Survival from Onset of Lymphangiosarcoma
Stewart and Treves (1948)	46	Left	Post-operative	8	Radiotherapy and surgery	Presumed dead
	60	Right	Pre-operative	8	Radical excision	?
	59	Left	Not noted	10	Amputation	20 mth.
	37	Right	Pre-operative	10	Amputation	8 mth. Pulmonary metastases
	40	Left	None	25	Radiotherapy followed by amputation	Alive at 14 mth. ? Pulmonary metastases
	36 50	Left Right, followed by œdema	None Pre-operative (pathology report benign)	6 yr. after mastectomy complicated by œdema, but 20 yr. since mastectomy for ? malignant lesion	Radiotherapy	4 mth. ? Pulmonary metastases
Ferraro (1950)	57	Left	Post-operative	9	Palliative	4 mth.
McCarthy and Pack (1950)	57	Right	Not noted	10	Palliative	Not noted
	59	?	Not noted	10	Amputation of arm	3 yr. and 5 mth. Pulmonary metastases
Cruse, Fisher, and Usher (1951)	53	Left	Pre-operative	12	Amputation	1 yr.
Froio and Kirkland (1952)	43	Left	Post-operative	11	Amputation	10 mth. Metastatic in lungs, bone, and tonsil
Jessner, Zak, and Rein (1952)	54	Left	Post-operative	7	Trial dose radiotherapy followed by amputation	15 mth. Recurrent at amputation site. Metastatic in lungs, bones, and lymph-nodes
Vos (1952)	41	Left	Not noted	14	Local excision and irradiation	Few months. Residual. Metastatic in lungs and bones
Hilfinger and Eberle (1953)	42	Bilateral, followed by œdema of right arm	Post-operative (L > R)	10	Amputation followed by palliative radiotherapy	11 mth. Recurrent at amputation site. Metastatic in lungs
	47	Left	Post-operative	16	Palliative radiotherapy	About 1 yr. Residual tumour. Metastatic in lungs and glands
Rawson and Frank (1953)	56	Left	Not noted	14	Radical radiotherapy	Still well at 2 yr. 8 mth.
Hall Smith and Haber (1954)	67	1. Left in 1949, followed by œdema 2. Right in 1952	Post-operative None	3 yr. since onset of œdema, but carcinoma of contralateral breast only 1 yr. previous	?	?
Bowers, Schear, and Le Golvan (1955)	41	Right	Post-operative	6	Forequarter amputation	Well at 2 yr.
Marshall (1955)	66	Right	None	5	Local excision followed several months later by amputation	18 mth.
Southwick and Slaughter (1955)	41	Left	None	8	Radical radiotherapy	Well at 6 yr.
Nelson and Morfit (1956)	68	Left	Post-operative	9	Radical radiotherapy	Well at 3 mth.
	62	Left	Not noted	9	Local excision and skin-grafts	3 mth. after operation metastatic in abdominal wall and lymph-gland. Alive
Kettle (1957)	63	Right	Post-operative	9	Local excision followed by radiotherapy	Alive at 1 yr. with local recurrence

excision and the amputation the patient developed an indurated 'bruise' 1·5 cm. diameter on the ventral aspect of her wrist.

The patient was reviewed at monthly intervals. In July, 1957, a few bluish raised nodules were noticed anteriorly to the operation scar. These were considered

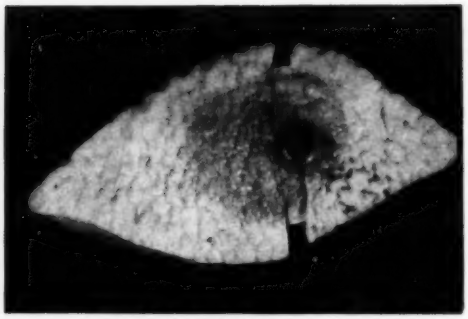

FIG. 341.—*Case* 2. Excised tumour. (× 2.)

FIG. 343.—*Case* 3. Showing œdema, tumour, bruises, and post-radiation changes.

evidence of recurrence but further surgery was not advised.

The recurrent tumours grew rapidly and within three months had almost completely covered the left side of the chest wall, spread across the posterior aspect of the right side of the chest and down the posterior aspect of the right upper arm. The tumours varied in size from minute petechial lesions to large fungating bluish-black masses formed by the fusion of adjacent lesions (*Fig.* 342).

A trial area on the anterior aspect of the chest wall was irradiated (500 r, 250 kV.), to test the radiosensitivity of the tumours. This resulted in ulceration of the treated area.

The patient died in November, 1957, 14 months after the first lesion was noted on her œdematous arm.

Case 3.—Mrs. J. P., aged 50 years, was referred to hospital with a lump in her left breast in March, 1948. A clinical diagnosis of carcinoma was made and she was treated by pre-operative radiotherapy and radical mastectomy.

Histological examination of the mastectomy specimen showed a scirrhous carcinoma without involvement of lymphatic glands. Fourteen days after the mastectomy persistent massive lymphœdema developed throughout the whole of the left arm. A partially successful attempt to relieve the œdema was made in December, 1949, by the insertion of nylon threads.

Apart from the œdema the patient remained well and free from any evidence of recurrent or metastatic carcinoma for 8 years. When seen in February, 1956, multiple subcutaneous hæmorrhages were noted on the left arm and in May, 1956, it was noted that these 'hæmorrhages' were indurated and raised.

FIG. 342.—*Case* 2. Appearance at autopsy, showing tumours and discoloration of the surrounding skin.

When seen by one of us in April, 1957, the left arm was grossly œdematous (maximum circumference of upper arm 40 cm.) with post-radiation pigmentation, papillomatosis, and atrophy of the skin over the upper inner aspect of the arm. Arising from the anterior aspect of the upper arm there was a tumour 4 cm. in diameter which the patient stated was of three weeks' duration. The peripheral part of the tumour was indurated and purplish in colour. The central part was slightly raised (0·75 cm.) above the peripheral component, reddish-brown in colour, with the surface bleeding and crusted. Farther down on the anteromedial aspect of the upper arm there were three bright-red indurated 'bruises', the largest 2·5 × 1·5 cm. in size. Four small vesicles about 3 mm. in diameter arose from the surface of the largest bruise (*Fig.* 343).

The clinical diagnosis of post-mastectomy angiosarcoma was confirmed by biopsy examination and a fore-quarter amputation was performed in June, 1957. At the time of writing there is no evidence of recurrence.

2. Early Lesions.—

Case 4.—Mrs. M. P., aged 53 years, was referred to hospital with a Stage 2 carcinoma of the left breast in February, 1950. She was treated by radical mastectomy followed by X-ray therapy to the supraclavicular area and axilla. Histological examination of the tumour showed it to be a cellular spheroidal-cell carcinoma, with a small deposit in an axillary gland. The patient's subsequent progress was uneventful apart from a moderate degree of lymphœdema in the left upper arm which had been persistent since 1950.

On examination in August, 1957, three small subcutaneous nodules were noted, one at the insertion of the deltoid muscle, and two a little lower down on the lateral aspect of the upper arm. The nodules were fixed to skin. Two months later the largest nodule was unchanged, the other two appeared to have regressed.

There was no evidence of local recurrence of the primary carcinoma on the chest wall, or of metastatic growth elsewhere. Radiography of the chest showed no evidence of malignancy.

Case 5.—Mrs. F. H., aged 46 years, was referred to hospital with a Stage 1 carcinoma of the left breast in March, 1945, and was treated by radical mastectomy and post-operative radiotherapy. Histological examination of the mastectomy specimen confirmed the diagnosis of

carcinoma, without involvement of the axillary glands. The patient remained well until April, 1949, when she noticed a lump in her right breast. A clinical diagnosis of carcinoma was made, and pre-operative radiotherapy was followed by a radical mastectomy. No histological evidence of malignancy was found in the mastectomy specimen. A moderate degree of persistent œdema of the right arm developed after the second mastectomy.

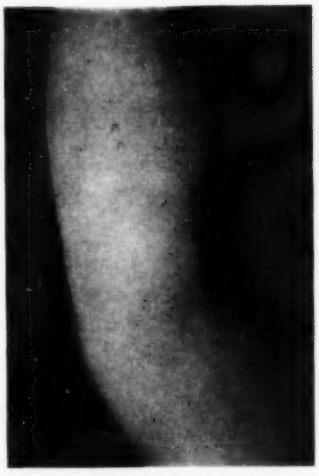

FIG. 344.—*Case* 4. Showing moderate œdema vesicles and bruising.

FIG. 345.—*Case* 2. Cut surface of tumour. (× 2.)

When seen in April, 1957, there was no evidence of any recurrence of the breast lesions. There was a moderate degree of brawny œdema of the right arm. Several small pale vesicles were arising from the medial aspect of the upper part of this arm, and on its anterolateral aspect there was an almond-shaped subcutaneous nodule, 2 cm. × 1 cm., which was fixed to the skin and surrounded by an area of yellowish pigmentation 6 cm. × 5 cm. (*Fig.* 344). The patient stated that she had first noticed this condition three years previously, and believed it to be unchanged since then.

We think that both of these patients are examples of a 'premalignant' phase in the development of an angiosarcoma, but in the light of present limited knowledge of this condition, it was felt that active radical treatment was not justified and the patients are being kept on a close follow-up.

PATHOLOGY

The material available for examination included the biopsy specimens from *Cases* 1–3; the amputated arms from *Cases* 2 and 3—these were cut tangentially at 4-cm. intervals; and the autopsy material from *Case* 2.

Blocks were prepared and serially sectioned from the obvious tumours, the 'bruises', the œdematous arms, and the autopsy material.

The macroscopical appearance of the arms indicated that the increase in their girth was due to a great increase in the subcutaneous fatty layer. Scattered in the skin and the underlying fat there were various lesions. Sometimes these appeared as areas of induration and hæmorrhage. Sometimes they were small masses of firm, pink tissue in the superficial 0·5 cm. of the subcutaneous fat, and with an area of 'bruising' in the overlying skin. In other places there were obvious tumours located primarily in the subcutaneous tissue; they had a firm red-brown cut surface in which areas of hæmorrhage were present (*Figs.* 345, 346). The larger tumours projected slightly through the skin, but most of their mass was in the subcutaneous tissue.

FIG. 346.—*Case* 3. Cut surface of tumour showing the bulk located in the subcutaneous tissue with the superficial part erupting through the skin.

Similar lesions, although on a much grosser scale, were present at the autopsy in *Case* 2. The normal subcutaneous and muscular structures of the left side of the chest wall were almost completely replaced by soft, confluent, hæmorrhagic tumours, which in some parts extended through the parietal pleura. Smaller tumours and areas of hæmorrhage were present in the subcutaneous tissue of the right side of the chest and the right upper arm.

The immediate cause of death in *Case* 2 was cardiac failure resulting from a large hæmorrhagic left-sided pleural effusion.

In spite of the enormous local spread of the tumours in the chest wall the only evidence of distant metastasis were small subpleural foci in the left lung which were possibly transpleural seedings rather than blood-borne metastases.

The Development of the Lesions.—From the histological study, a general picture can be drawn of the course of development of the lesions, from the very earliest stages up to the full angiosarcoma. In the following account, this development will, for convenience, be divided into three stages, but each stage merges gradually into the next one, and many different stages can be seen in neighbouring parts of the same arm.

Stage 1 : *A Prolonged Lymphœdema.*—The essential feature of this stage is a widespread œdema and degeneration of the collagen tissue and fat in the dermis and subcutaneous tissue.

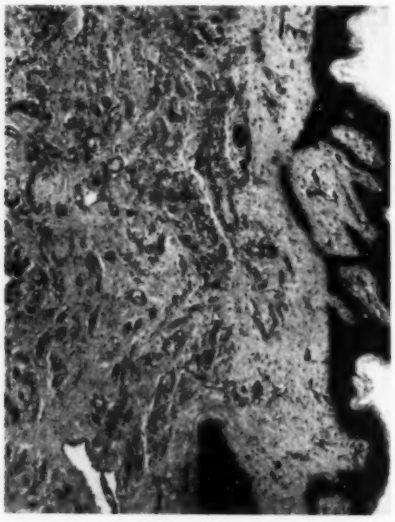

FIG. 347.—*Case* 3. Capillary hæmangiomatous infiltration of dermis and subcutaneous tissue. (× 64.)

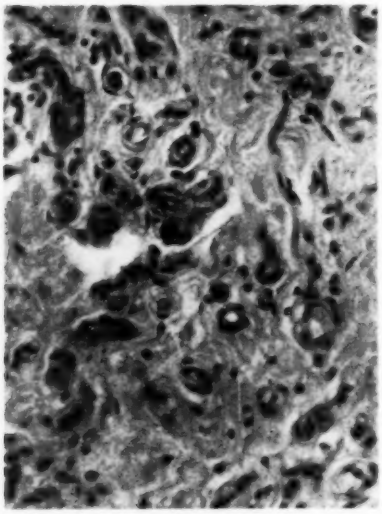

FIG. 348.—As *Fig.* 347, to show the structure of the well-developed vessels. (× 256.)

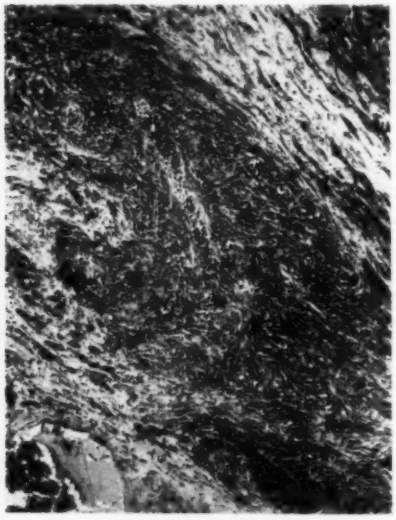

FIG. 349.—*Case* 3. Fibromatous-like area in the subcutaneous tissue. (× 64.)

The œdema gives rise to much separation of the collagen bands in the dermis and the subcutaneous tissue, and this produces an apparent increase in the amount of fibrous tissue there. There is probably no true increase in the amount of fibrous tissue.

The degenerative changes are most marked in the deeper dermis and the subcutaneous tissue. The normal structure of the interlobular fibrous septa in the subcutaneous tissue is replaced by an acellular fibrin-like network. In small patches in the subcutaneous tissue and around the base of the sweat glands, there is a striking œdema and degeneration of the fat cells which give rise to large irregular cavernous spaces. Around many of the small dermal blood-vessels there is some perivascular lymphocytic cuffing.

Stage 2 : *Pre-malignant Angiomatosis.*—The characteristic change in this stage is a proliferation of small vessels in the dermis and subcutaneous tissue in numerous foci throughout the arm. Histologically these are seen as small channels lined by hyperplastic endothelial cells, contrasting with the flattened endothelial cells of the more normal vessels. Many of these proliferating vessels appear to be arising from lymphatics, but others were filled with red corpuscles and were presumably arising from blood capillaries.

These foci of angiomatosis vary in size from 100 μ to several centimetres in diameter. The more superficial areas are manifest on the surface as bruises or as vesicles; the deeper ones correspond with the

areas of induration and hæmorrhage observed with the naked eye in the subcutaneous tissue; the smaller ones are only evident microscopically.

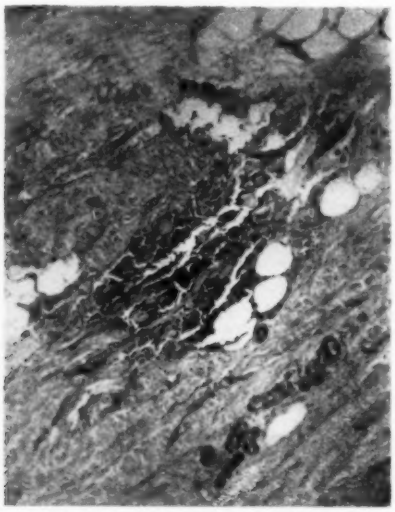

FIG. 350.—*Case* 2. Small focus of proliferating vessels and lymphocytes infiltrating the dermal collagen, suggestive of carcinoma. (× 64.)

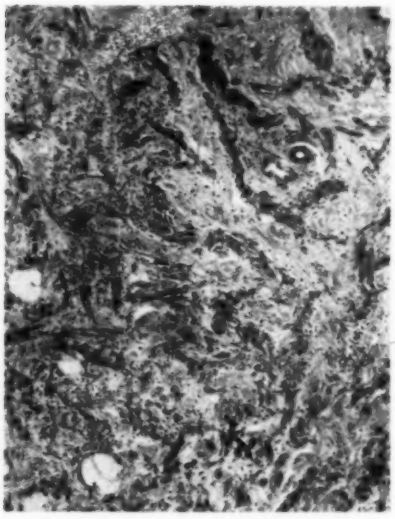

FIG. 352.—*Case* 3. Transition stage between 'angiomatous' and 'fibromatous' areas, with cords of endothelial cells, accompanied by lymphocytes infiltrating the dermal collagen. (× 64.)

Sometimes the vessels form an anastomosing plexus of capillary and cavernous spaces (*Figs.* 347, 348) which communicate with small, subepithelial pedunculated angiomas. Sometimes the hyperplastic endothelial cells, (*a*) form masses of spindle cells which on close inspection are suggestive of soft fibromata (*Fig.* 349), or (*b*) infiltrate between neighbouring collagen bundles giving an appearance reminiscent of secondary carcinoma (*Figs.* 350, 351).

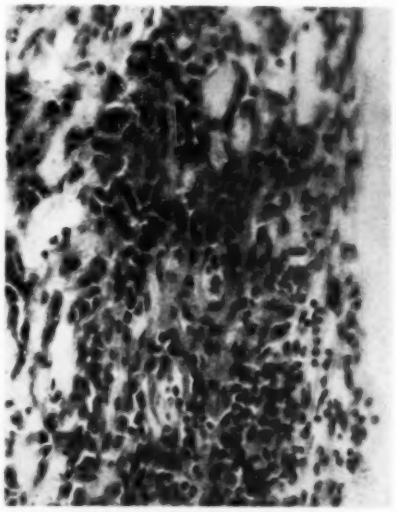

FIG. 351.—As *Fig.* 350, showing the proliferating lymph-vessels. (× 256.)

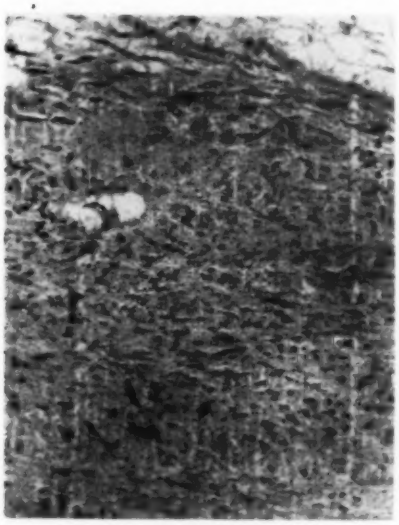

FIG. 353.—*Case* 2. Infiltration of subcutaneous connective tissue by small proliferating vessels. (× 64.)

Careful examination shows, however, that many of the cells are lining narrow channels, and transition stages from the more obvious angiomas can always be found (*Figs.* 352–354).

The proliferating vessels are frequently accompanied by lymphocytic infiltration, but this does not

appear to be an essential part of the process. Infiltration into areas of degenerate fat is often accompanied by fairly extensive hæmorrhage.

Although in some of these lesions there is little evidence of malignancy, the more advanced lesions show what must be considered as early malignant angiosarcomas. They arise multifocally from areas of premalignant angiomatosis which can sometimes be observed at the periphery of the tumour (*Fig.* 355).

Histologically any single tumour may show a range of cellular type. At one end of the scale the

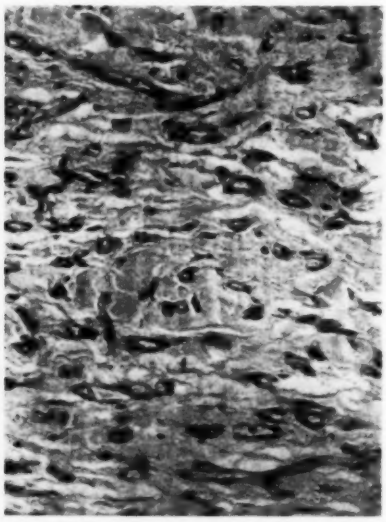

FIG. 354.—As *Fig.* 353, showing the primitive structure of the vessels. (× 256.)

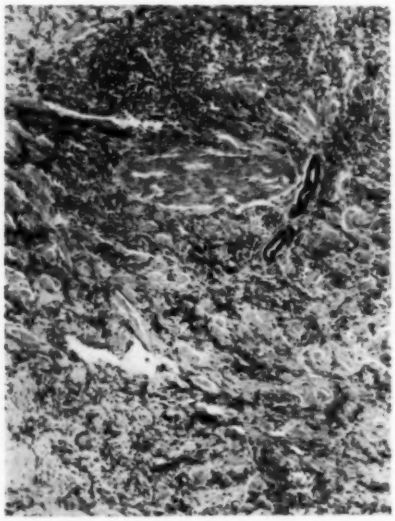

FIG. 355.—*Case* 2. Peripheral part of tumour; note the similarity to *Fig.* 351. (× 64.)

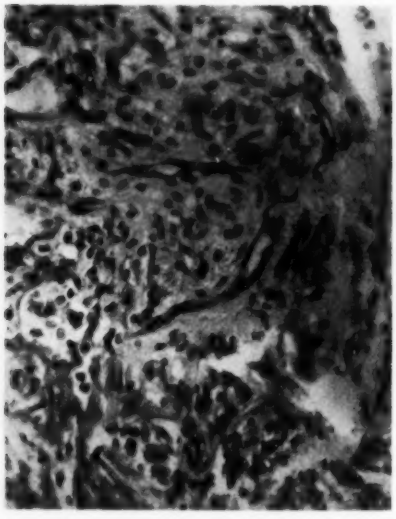

FIG. 356.—*Case* 1. Area of tumour showing vasoformation. (× 256.)

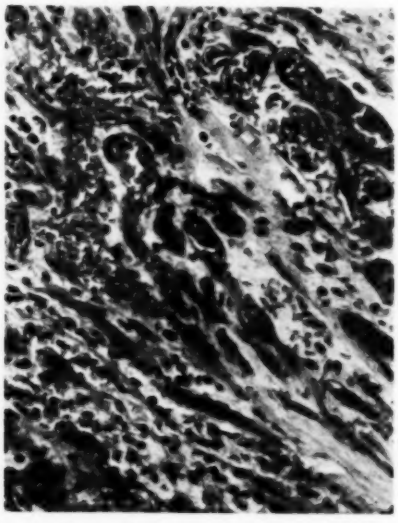

FIG. 357.—*Case* 2. Section showing bizarre endothelial cells forming channels containing red blood-cells. (× 256.)

changes, with mitotic figures and cellular pleomorphism.

Stage 3: *Frankly Malignant Angiosarcoma.*—These tumours are rapidly growing pleomorphic vascular nature of the tumour is obvious. Bizarre vascular channels, lined by pleomorphic malignant endothelial cells, frequently containing red corpuscles, infiltrate the adjacent tissue (*Figs.* 356, 357). At the

other end there is no evidence of any vasoformation and the tumour consists of (*a*) spindle cells with deeply staining nuclei and scanty cytoplasm (*Fig.* 358) or (*b*) large cells with large leptochromatic nuclei with a single nucleolus and abundant cytoplasm; the cellular outlines may be fairly clear so that the cells resemble reticulum cells, or they may be quite indefinite so that the cells form a syncytium which may resemble an anaplastic carcinoma (*Fig.* 359).

In some of the cellular parts of the tumour there is extensive vacuolation of the cytoplasm and disruption of the cells to form irregular channels lined by a single layer of flattened nuclei and containing red corpuscles. In other parts of the tumour there is widespread extravasation of red corpuscles and also infiltration of lymphocytes. This often extends out into the adjacent tissue.

The walls of veins in the neighbourhood of these tumours are often replaced by tumour cells and lymphocytes, but the lumen is not invaded. The malignant change appeared to arise within the vein wall, possibly from the vasa vasorum or lymphatics (*Figs.* 360, 361).

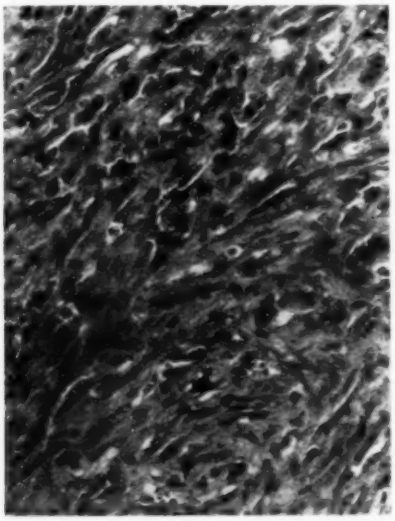

FIG. 358.—*Case* 3. Spindle-cell sarcoma area of tumour. (× 256.)

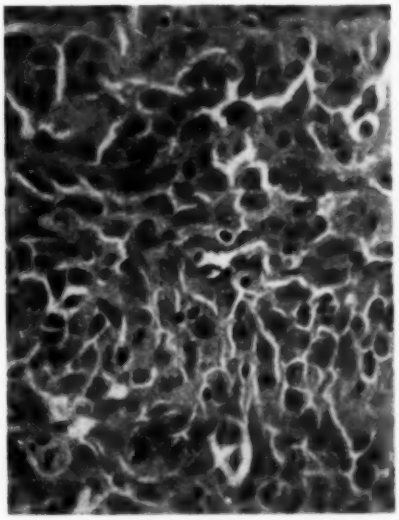

FIG. 359.—*Case* 2. Anaplastic carcinoma-like area of tumour. (× 424.)

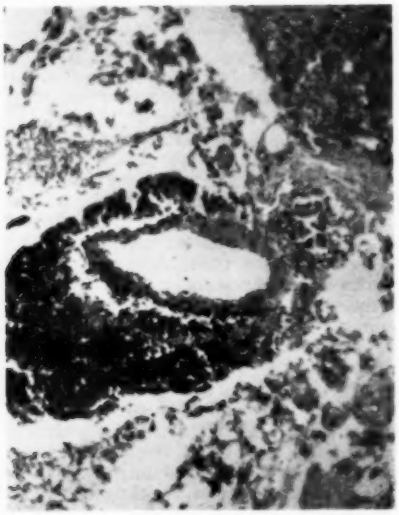

FIG. 360.—*Case* 2. Section showing replacement of vein-wall by lymphocytes and tumour. (× 64.)

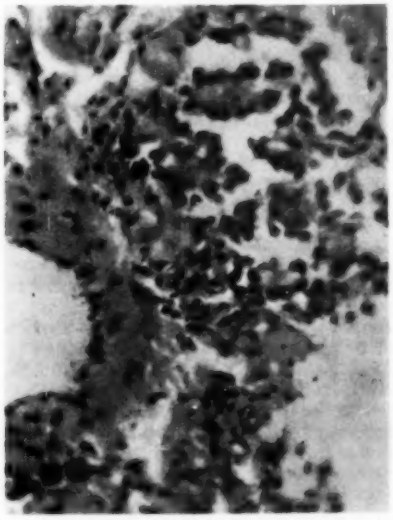

FIG. 361.—As *Fig.* 360, to show small focus of papilliferous tumour growing from vein wall. (× 256.)

Conclusion.—

From the histology there is no doubt that the amputated arms in *Cases* 2 and 3, and subsequently the chest wall and right arm in *Case* 2, were the site of very numerous foci of angiomatosis. At the time of amputation only a small proportion of these foci in the arms had become frankly malignant angiosarcomas; however in *Case* 2 at the time of death the malignant change in the tissues of the chest wall completely overshadowed the angiomatosis. There can be no doubt that if amputation had not been performed a similar widespread malignant change would have occurred in the arms; it is clear, therefore, that the local treatment of those tumours which are obvious to the naked eye is useless.

It is an interesting fact that the series of lesions appear to originate in the deep dermis and in the subcutaneous tissue or occasionally in the outer part of the deep fascia. No satisfactory explanations can be offered for the fact that none of these series of lesions arises from fibrous tissue of the intermuscular septa, although in *Case* 2 larger tumours invaded and replaced the muscle.

DISCUSSION

Post-mastectomy angiosarcoma is now established as a definite complication of post-mastectomy lymphœdema. Though it is usually considered an uncommon condition, it has been suggested that its rarity is apparent rather than real, the tumours being misdiagnosed as recurrences of mammary carcinoma. In an attempt to assess the frequency of the condition the records of 894 cases of carcinoma of the breast registered with Merseyside Cancer Control Organization during the years 1944–1950, treated by radical surgery with or without radiotherapy and having a minimum of 5 years' survival time, were examined. In this series 3 definite and 2 early lymphangiosarcomas have occurred (one histologically proven case was originally misdiagnosed as a recurrence of the mammary carcinoma), an incidence of 0·45 per cent. This may be too low a figure, as the average cancer-free latent period in published cases is 10 years and it is thus quite possible that additional cases will occur within the next few years.

It was unfortunately not possible to estimate the incidence of post-mastectomy lymphœdema in this series as only the more severe degrees of œdema are noted; however, 4 of the cases of angiosarcoma reported in this paper occurred in a group of 45 patients in whom the degree of œdema had been sufficient to have merited a note on the case sheet. It is probably correct to assume that it is the patients with moderate and severe œdema who are most likely to develop post-mastectomy angiosarcoma, and that in these patients the incidence of angiosarcoma is in the region of 10 per cent or more.

In our records of patients known to have survived 5 years after mastectomy for carcinoma of the breast there is no example of secondary carcinoma developing in the arm; thus in these cases lymphangiosarcoma would appear to be commoner.

The condition occurs in late middle age, the recorded cases varying between 49 and 77 years of age. This of course follows the high incidence of carcinoma of the breast in patients of the 40–60 age group.

An operation on the left breast appears to be more likely to be complicated by an angiosarcoma than one on the right side—14 previously reported cases have been on the left side, 8 on the right, and in the remaining case the side was not noted. The 3 definite and 1 of the early cases reported in this paper occurred on the left side; the other early case was on the right side. It is possible that for anatomical reasons a left radical mastectomy is more likely to be complicated by severe lymphœdema than a right-sided operation. This is borne out to a certain extent by the fact that of the 45 patients with severe lymphœdema 26 followed a left mastectomy and 19 a right mastectomy.

The better prognosis and longer expectation of life in those patients with carcinoma of the breast in whom the axillary nodes are free from metastatic growth is reflected in the finding that the patients who subsequently develop post-mastectomy angiosarcomas mostly come into this group. In the previously recorded cases histological involvement of the axillary nodes was noted in 2 cases; in 11 cases the nodes were recorded as being free from tumour; and in the remaining 9 cases the state of the axillary nodes was not noted. In the cases recorded in this paper 1 case showed histological evidence of early involvement of an axillary node (*Case* 4).

The role of radiotherapy in the aetiology of post-mastectomy angiosarcoma is difficult to assess. It is obviously not an essential factor as 3 of the previously recorded cases had not received any form of radiotherapy (*see Table I*). In 6 cases radiotherapy was not noted in the records. The remaining 14 cases and the 5 cases reported in this paper all received radiotherapy, 6 pre-operatively and 13 post-operatively. Treves (1957), from a study of the incidence of lymphœdema in a series of 3013 cases of carcinoma of the breast treated by radical mastectomy, wrote: "the most striking factor associated with post-mastectomy swollen arm was irradiation". If this is so then radiotherapy, by increasing the incidence of post-mastectomy œdema, could be regarded as a contributory factor to the development of post-mastectomy angiosarcoma.

When an angiosarcoma arises in a lymphœdematous extremity the prognosis is very poor. Of the 18 cases recorded in the literature in which the subsequent course is unknown, 7 died in the first year, 5 died in the second year, and 1 in the fourth; 2 were suffering from recurrences when reported during the second year, and 3 were apparently well after 2, 2½, and 6 years. The tumour metastasizes very early via the blood-stream to the lungs, pulmonary metastases being noted in 9 cases, and also in *Case* 1 described in this paper. Additional metastatic deposits were also noted in bones (3 cases), lymph-nodes (2 cases), and in 1 case in the tonsil.

The tumours are usually regarded as lymphangiosarcomas, although Hilfinger and Eberle (1953) raised the possibility of a dual origin from both lymphatic and blood-vessels. This view is supported in the present series. In each case there was undoubted malignant proliferation of lymphatic vessels. In *Case* 3 there was also a multifocal proliferation of blood-vessels, at a distance from the main tumour; and in *Case* 2 the tumour appeared to stimulate the overproduction of capillary blood-vessels in its

immediate vicinity, the resultant appearances being reminiscent of malignant granulation tissue.

From a study of the histological material in the cases recorded in this paper it appears as though the first stage in the evolution of the condition is œdema and widespread degeneration of subcutaneous and dermal collagen and to a lesser extent degeneration of fatty tissue, accompanied by lymphocytic cuffing of small blood-vessels, particularly those at the lower edge of the dermis. This is followed by a multifocal proliferation of endothelial cells in the lower dermis and subcutaneous tissue, which in the larger and also more superficial areas correspond with external evidence of 'bruising'. It appears possible that at this phase the endothelial proliferation may represent a premalignant angiomatosis which is followed, usually fairly quickly, by the frankly malignant angiosarcoma. If this is so it seems highly probable that the lesions in *Cases* 4 and 5 correspond to this premalignant phase, but in which the malignant transformation has not yet occurred. The cases reported by Jessner, Zak, and Rein (1952), and by Bowers, Schear, and Le Golvan (1955), support the hypothesis of a premalignant phase in the evolution of post-mastectomy angiosarcoma. In these 2 cases 6 months and 1 year respectively elapsed between biopsies which demonstrated benign vascular tumours and those showing malignant lymphangiosarcomas.

The relationship between long-standing œdema and the development of malignancy is obscure. Although the massive hyperplasia of connective tissue which occurs in tropical elephantiasis has been appreciated for a long time to be due to the blockage of lymphatic vessels by filaria and allied parasites, it is not generally believed that long-standing œdema *per se* predisposes to the development of malignancy. Martorell (1951) drew attention to the fact that lymphœdema, as opposed to venous œdema, excites fibroblastic proliferation and possibly also neoplasia. He describes a patient in whom 'essential' lymphœdema of the lower extremities was complicated by the development of an angiosarcoma which recurred and metastasized after treatment by means of local excision and radiotherapy. There are several other cases recorded in the literature in which angiosarcomas have arisen in lymphœdematous extremities in the absence of any previous history of malignancy.

Kettle (1918) described a patient in whom congenital elephantiasis of the right leg was complicated when the patient was 44 years of age by the development of an angiosarcoma.

Raven and Christie (1954) described the development of an angiosarcoma in a woman 61 years of age. She had plastic surgical treatment for an extensive congenital nævus of the left arm, but the arm remained grossly swollen, and when seen by them it was the site of a large ulcerated angiosarcoma. The tumour metastasized to the lungs and liver.

Aird, Weinbren, and Walter (1956) have recently published a case of angiosarcoma complicating spontaneous lymphœdema. The patient, a female, developed spontaneous lymphœdema of both legs at the age of 49. This persisted and eight years later was complicated by the development of an hæmangiosarcoma on the right leg. Combined surgical and radiotherapeutic treatment was given but the patient died within 3 years, the tumour being recurrent locally and also metastatic in the lungs.

The relationship between œdema and the development of Kaposi's disease is difficult to assess. It is possible to divide the cases recorded as Kaposi's disease into two groups:—

1. The great majority of cases conform with the generally accepted picture of Kaposi's disease with symmetrical, hæmorrhagic, granulomatous tumours of the extremities which frequently undergo spontaneous regression. These lesions are accompanied or followed by œdema. The condition is of long duration and usually occurs in males (Tedeschi, Folsom, and Carnicelli, 1946, in a survey of 434 cases found an incidence of 94 per cent in males). An uncommon late complication is the development of fibrosarcoma.

2. In a small group of atypical cases the earliest manifestation is œdema, which precedes by several years the development of a rapidly progressive angiosarcoma. These cases will be described in greater detail:—

a. Hansson (1940) recorded a case in a female who developed spontaneous œdema of the right leg which persisted in spite of plastic operations. Nine years later small reddish-blue skin tumours developed on the lower part of the œdematous leg, necessitating amputation. Histological examination showed a malignant vascular sarcoma.

b. Aegerter and Peale (1942) described a similar case again in a female who had developed persistent œdema of the right leg following a plastic operation at the age of 11 years for the removal of a simple angioma situated above the knee. At the age of 40 she developed 'inflammation and discoloration' of the right second toe, which was amputated. Histological examination showed an angiosarcoma. The tumour spread and involved the rest of the œdematous leg.

c. Stats (1946) considers that swelling of the extremities may often be the first manifestation of Kaposi's sarcoma. He described 3 patients (2 female, 1 male) in whom severe œdema of the legs had preceded by periods varying between 2 and 10 years the development of skin lesions which were first manifest in the œdematous legs. The disease in these patients progressed rapidly after the onset of the primary skin lesions, metastasizing widely to other parts including the skin of the rest of the body, lymph-nodes, lungs, and alimentary tract.

These 5 cases appear to be comparable with the cases of angiosarcomas developing in lymphœdematous extremities reported by Martorell (1951) and by Aird and others (1956), rather than with the usually accepted concept of Kaposi's disease.

In the light of the above 9 cases in which angiosarcomas developed in lymphœdematous extremities in the absence of any previous malignancy, it is possible that the development of post-mastectomy angiosarcoma is not due to a general systemic carcinogen as was suggested by Stewart and Treves (1948), but is due to a direct relationship between long-standing œdema and angiosarcoma, the treatment of carcinoma of the breast unfortunately providing in some cases a mechanism for producing severe, permanent lymphœdema of the arm.

It is interesting to speculate as to whether the œdema fluid itself is carcinogenic or whether the malignant change is associated with the widespread degeneration particularly of collagen but also of fat. That atrophy and degeneration can give rise to malignancy after a long latent period is borne out by the late development of squamous carcinomas in the atrophic skin following burning, lupus, or excessive radiotherapy, and it seems possible that the long-continued degeneration resulting from the severe lymphœdema may stimulate the development of a malignant connective-tissue lesion. Why the lesion should be angiosarcomatous in type is difficult to understand, but there seems to be no doubt that the lesion takes origin from small vessels whether they be lymphatic or blood in type.

It is difficult with so few cases to assess the value of any particular form of treatment for post-mastectomy angiosarcoma. Any measures which will reduce the incidence of post-mastectomy lymph-œdema will of course lessen the incidence of post-mastectomy angiosarcoma. Early diagnosis of angiosarcoma is essential for the success of any mode of therapy as local spread and blood-borne metastases occur so readily. The patients at risk are largely those in whom local recurrence of the original malignant lesion is considered to be unlikely and consequently are on a yearly follow-up. It seems desirable that patients with post-mastectomy lymph-œdema of over 7 years' duration are kept under more frequent supervision.

Radiotherapy and radical surgery have both been employed in treatment, and of the 5 recorded cases free from recurrence of angiosarcoma at 12 months, 2 had been treated by radiotherapy and 3 by amputation of the arm. The longest survival is in the case described by Southwick and Slaughter (1955); their patient is still well 6 years after treatment by radical radiotherapy. Clinically this appears to have been an early lesion and the accompanying microphotograph shows an appearance similar to the 'premalignant angiomatosis' described in this paper, rather than to the fully developed malignant angiosarcoma. The case described by Rawson and Frank (1953) was well 2 years 8 months after radiotherapeutic treatment. McCarthy and Pack (1950) and Stewart and Treves (1948) described cases surviving 3 years 5 months and 1 year 8 months respectively after amputation of the arm—death resulting in each case from pulmonary metastases.

SUMMARY

Three cases of malignant post-mastectomy angiosarcoma and 2 premalignant cases are recorded. The patients all gave the typical history of having had a radical mastectomy for carcinoma of the breast which was complicated by a moderate or severe lymphœdema of the arm. After an average latent period of 8 years they developed small subcutaneous nodules and 'bruises' on the œdematous arm. These lesions correspond histologically with multifocal foci of endothelial proliferation, involving both lymphatic and blood-vessels. This pre-malignant angiomatosis is followed, usually within a few months, by the development of frankly malignant angiosarcomas. The prognosis of post-mastectomy angiosarcomas is very bad, their multifocal origin leading to a rapid local spread, and metastasis via the blood-stream occurring early. Long-standing lymphœdema rather than a malignant diathesis is probably the important aetiological factor; the relationship between œdema and the development of malignancy is discussed.

The recorded cases have been treated either by radiotherapy or by amputation of the arm.

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A METHOD OF CAROTID LIGATION

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THE PROBLEM

Owing to the increasing demand for neurosurgical attention to cerebral aneurysms there is a growing need for safer methods of carotid ligature. Cerebral anoxia remains an ever-present danger.

Indeed, in ligating the parent vessel of an aneurysm generations of surgeons have attempted to free the assets of cure from the liability to ischæmic changes. Thus, it was probably Deschamps (1797) who first suggested gradual arterial closure to encourage collateral circulation: thirteen years later Dubois (1810) applied that to the treatment of aneurysms. Many techniques such as Keen's screw clamp (1900) and Matas's (1911) aluminium clips have since been developed to achieve a gradual or partial occlusion. More recently Pearse (1940) has employed cellophane slowly to constrict the aorta and carotid arteries.

Despite measures to augment collateral flow, however, cerebral ischæmia and hemiplegia may still follow interference with the carotid circulation. The risk is less when the external carotid anastomoses are preserved by ligating the common instead of the internal carotid artery (Schorstein, 1940): it is further reduced if one first ascertains that a temporary occlusion is tolerated before the ligature is tied (Rogers, 1949). Our safeguards must remain inadequate, however, because no measures at the outset can guarantee a permanent sufficiency of cerebral blood. For example, variations in either the cardiac output or calibre of the remaining arteries to the neck and brain carry some risk of delayed cerebral damage. Whatever the cause, neurosurgical experience (Johnson, 1952) shows that the more remote prognosis is largely determined by what happens in the first forty-eight hours. Indeed, Le Fort (1868) commented on the delayed onset of hemiplegia after carotid ligature and drew particular attention to the second post-operative day as the most critical period. Thus, a method of restoring the patency of a carotid artery within the first forty-eight hours of its occlusion should both cover the period of maximum importance and provide a safety measure if cerebral function fails. This communication has in fact been stimulated by 3 instances of hemiparesis that presented within forty-eight hours of common carotid ligature. Although it was possible to remove promptly the ligatures the satisfactory functional recovery of each patient was known to be fortunate. The removal of a simple metal clip such as Matas's (1934) is quicker and safer than ligature removal: release of a screw clip such as Selverstone's (1957) is better still. Some surgeons, however, still fear late secondary hæmorrhage as a complication from the permanent application of metal devices to the larger arteries. Halsted (1905) originated an aluminium band for the purpose. He reported, "The experimental work on animals has led me to expect that ultimately the metal band must cut through the artery".

THE METHOD

The object of this report is to present a method of carotid ligature that reduces the risks of cerebral anoxia in the first two post-operative days. At first a simple screw clip is applied which, after a trial period of obstructing one common carotid artery for two days, is removed at a second stage when definitive ligation is performed.

Indications.—The method has principally been used in cases of cerebral aneurysm. It has been resorted to where the risk of anoxic brain damage has seemed exceptionally great. For example, although a patient who is in coma with subarachnoid hæmorrhage does not tolerate a carotid ligature, one who is partly conscious may. On the other hand there may be evidence of active bleeding from an aneurysm, yet the patient is fully conscious. Due to the vagaries of the aneurysm, however, coma can suddenly follow. A method for re-starting as well as stopping the circulation within one common carotid artery contributes to the management of such problems. Thereby some lives may be saved by stopping aneurysmal bleeding while the dangers of deteriorating consciousness and hemiplegia are very greatly reduced. Again, in the neurosurgery of aneurysms there are familiar angiographic appearances that suggest a cerebral blood-supply of doubtful adequacy. Arterial spasms may indicate a marked regional ischæmia. Or compression of one common carotid artery may fail to demonstrate passage of the contrast medium across the anterior communicating artery from the injected side to the other. Indeed, both anterior cerebral arteries may appear to fill from only one side. To some extent the true dynamics in the circle of Willis must remain equivocal unless the contribution from the vertebral as well as from the carotid systems is known. But as there are signs clinically so there are appearances angiographically to indicate that carotid ligature may not only thrombose a particular aneurysm but also seriously harm the patient. The same consideration must be given to general disorders that can the more readily lead to ischæmic brain disease when a carotid artery is tied. Thus degenerative vascular disease and vascular hypertension, possible narrowing of the vertebral as well as of the carotid trunks (Hutchinson and Yates, 1957), cardiac irregularities (Eastcott, Pickering, and Rob, 1954), or anæmia may prohibit permanent closure of one common carotid vessel.

Uses.—Initially therefore the writer's screw clip with the procedure of two-stage ligation was used in the treatment of cerebral aneurysm. These were individual problems where a direct approach procedure was not feasible. In addition to the variable features of actual subarachnoid hæmorrhage already alluded to, particular groups of aneurysm problems have emerged which appear well suited to this method. Thus, there are those who present with active expansion and threatened rupture of an aneurysm

(Jefferson, 1938). They come with warning head pains, often frontal or in relation to one eye, and frequently with a developing third-nerve paralysis. It is due to a risk of sudden hæmorrhage with coma in such cases that the screw clip has been preferred in the first place to one-stage ligature. A further group comprises those patients with subarachnoid hæmorrhage who, in the absence of an intracranial

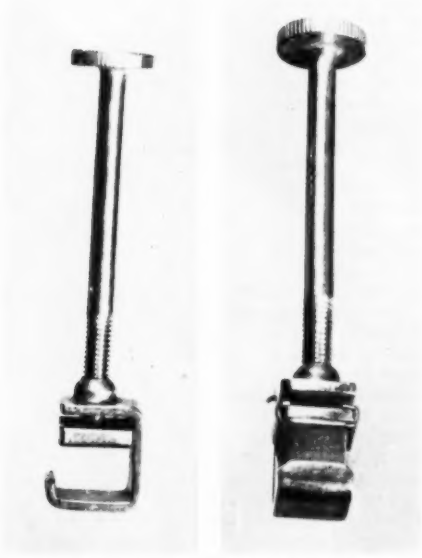

FIG. 362.—The carotid screw-clip. (Actual size.)

clot, exhibit a hemiparesis. This may vary from a hyper-reflexia and extensor plantar response to definite unilateral weakness. These people can be made hemiplegic by a carotid ligature: they may die if left untreated. Reference has been made to the older group of patients who, with cardiovascular disease, are more wisely treated with a trial period of carotid occlusion when cerebral aneurysm endangers life and cannot be attacked intracranially.

This screw device for two-stage carotid ligature has been extended to include all cases requiring interruption of a common carotid vessel where the threat of hemiplegia has been a special hazard. Recurrent copious hæmorrhage from traumatic rupture of an internal carotid vessel into the sphenoidal air sinus and carotico-cavernous fistula have accordingly been treated. In addition the screw clip has been put to further use as a prophylactic measure in the brain surgery of vascular lesions. Thus in difficult procedures it has been placed loosely around the common carotid artery as a safe-guard additional to hypotension.

Screw-clip Manufacture.—No special facilities are required to make the screw clip (*Fig.* 362). I adapted it originally from the screw clamp provided for the tubing of British transfusion sets. The essential requirement of a 2-in. stem is met by welding a longer piece on to the existing one. That is mounted with a suitably milled disk for a handle. The jaws may with advantage be reduced a little in size. The importance of smooth surfaces to embrace the common carotid artery is obvious, and for that reason it is well to fit a thin metal plate over the moving half of the jaw so that the revolving screw insert does not abraid the vessel wall. Owing to the short period the screw clip lies in the tissues no specially inert materials are employed: stainless steel is satisfactory.

Operative Technique and Management.—In the application of this instrument local anæsthesia is employed so that the patient may be spoken to and examined during closure of the screw. Certain points of actual technique may be mentioned. Through the crease incision centred on the edge of the sternomastoid muscle it is important to clear not less than 4 cm. of common carotid from its sheath and adventitious coat. A shorter artery length cramps the second-stage operation. For the same reason the clip should be placed on the lowest centimetre of exposed vessel. The screw clip is closed just to a point where the distal pulse is felt to fall suddenly by direct finger palpation within the wound. Any other estimate of closure such as that from increasing resistance to turning the screw clip could damage the artery. Having gently occluded the artery the patient remains in the operating room for half an hour and is then examined neurologically to ensure that there are no signs of cerebral ischæmia. In conclusion petroleum jelly gauze is lightly packed on all sides of the stem of the screw to keep the tissues, and especially the skin, from touching it. I prefer an everting stitch to the skin edges on either side to guarantee the immunity of the epithelium from contact with the protruding foreign body. A light dressing is perforated for the stem of the instrument, while over the flat head of the stem a piece of gauze is laid, adherent to the middle third of an Elastoplast strip. On return to the ward a diagram of the screw with its turning directions is explained to the nurses. They are also briefed with regard to the levels of consciousness and to the first signs of hemiparesis or dysphasia. Those observations are added to the customary half-hourly craniotomy check and special reference is also made to guarding against any fall in blood-pressure or cardiac irregularities. The patient is nursed supine and provided with a bell on that side not threatened by hemiplegia. He is instructed to call or ring should any untoward difficulty or feeling affect his limbs or speech. Symptoms or signs are at once reported to the medical staff. Should there be unmistakable features of hemiplegia anyone in an emergency can lift back the dressing and reopen the carotid artery by anticlockwise turning of the screw. With the average thread about four revolutions restore good patency and that can be confirmed by feeling strong pulsations in the neck distal to the dressing.

In the absence of any signs due to cerebral ischæmia the clip is replaced by ligature in continuity on the third day. This may be most safely performed under local anæsthesia. This is at least uncomfortable, however, and light general anæsthesia may be used provided early waking in the operating room is assured. Technically it is necessary to clear the fibrinous exudate from the full length of the previously

exposed carotid artery in order to ligate the vessel before removing the screw clip. The wound is subsequently closed with sutures to platysma and either Michel clips or sutures to the skin.

Initially the clip was gradually closed during the two days that followed its application. Because the most dangerous time after total carotid occlusion is the second day, however, complete closure from the outset is now preferred. It is felt that once the second post-operative day has passed the risk of hemiplegia diminishes while that of embolism from manipulation at the second operation becomes greater.

RESULTS

On 28 occasions I have employed this screw-clip device. Beyond one case of basal fracture associated with internal carotid rupture and another of traumatic carotico-cavernous fistula, all have been for berry aneurysm. One-half of those aneurysms involved technically difficult direct approach procedures in which the screw clip lightly held the common carotid artery during craniotomy. Had there been a serious intracranial hæmorrhage at operation, the clip would have been temporarily closed in an effort to reduce bleeding.

The remainder required common carotid ligature, but the risk of cerebral damage was sufficient in each case to contra-indicate the customary one-stage operation. The screw clip was accordingly used with formal ligation of the common carotid artery at a second stage. This practice has not met with a mortality or any instance of residual hemiplegia during the two-year period that I have used it.

Complications.—One patient showed to an alert nurse signs of commencing hemiplegia on the second night. The clip was quickly unscrewed and function completely returned. Two patients who were desperately ill with active aneurysmal bleeding developed a variable weakness of the contralateral limbs some days after the second-stage ligature. Both recovered fully.

On removal of the screw clips a close inspection of each common carotid artery has revealed no instance of bruising or other sign of vascular damage. Cultures taken from fibrin within the wound at the second operation have been sterile. Routine antibiotic cover has not been resorted to and in each case there has been healing by first intention following the delayed primary suture. One wound, however, became superficially and mildly infected in a patient who persistently scratched her neck.

With the adoption of this two-stage ligature for cerebral aneurysm in other centres, there have been 3 occasions on which colleagues have brought unfavourable results to my notice. In one case infection occurred in a neck wound where the edges approximated the shaft of the screw—the soft tissues and the skin having been left in contact with it. In another hemiplegia developed on the fifth day. The third misfortune was a hemiplegia that complicated the second operation. On that occasion removal of the screw clip preceded application of the ligature. When hemiplegia was observed it was attributed to embolism and the ligature left in position.

CONCLUSION

An arterial screw clip is described with special reference to its use in ligature of the common carotid artery by a two-stage method. That method may be an advance in reducing the risk of cerebral anoxia and hemiplegia.

Acknowledgements.—I wish to thank particularly Mr. R. T. Johnson, in whose Department at the Manchester Royal Infirmary, England, most of this work was done. In the principles of the management of cerebral aneurysm I owe much to him and to Sir Geoffrey Jefferson.

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THE INDICATIONS FOR AND LIMITATIONS OF FROZEN SECTION DIAGNOSIS

A REVIEW OF 1269 CONSECUTIVE FROZEN SECTION DIAGNOSES

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INTRODUCTION

Frozen section diagnosis has now reached a high level of accuracy. We propose to review 1269 consecutive frozen sections on different organs and briefly discuss the indications for, and limitations of, the method. It is proposed to take each organ separately and make comments as to the value and limitations of frozen section in the organ under discussion. Representative examples and problem cases will be cited with appropriate illustrations. This method of diagnosis is used more often in the United States than in any other country. We believe, however, that there are few centres that are utilizing this form of diagnosis to its fullest possible extent. There are several reasons why the method has not been fully exploited. The pathologist may not have had the experience in doing frozen sections or the surgeon may not have confidence in his diagnosis. Furthermore, in many institutions frozen section diagnosis has been delegated to relatively inexperienced men. We believe that the responsibility of frozen section diagnosis should be that of a senior pathologist and such a man should be rich in experience, conservative in attitude, and, most important, he must have judgement. We are not in favour of using the pathologist as a technician in order to satisfy the surgeon's intellectual curiosity or to prove that there is a pathologist in the hospital. Frozen section diagnosis should not be a method used routinely in every specimen removed at the operating table, but should be reserved for those instances in which a therapeutic decision has to be made.

THE PURPOSE OF FROZEN SECTION DIAGNOSIS

The purpose of the frozen section is sometimes lost in the drama and nervous tension often present in the operating room. There is really one purpose in the frozen section and that is *to make a therapeutic decision*. Although exact histologic diagnosis is much to be desired, in most instances it is sufficient to know that the lesion present is a malignant tumour or a non-neoplastic lesion, for it is on the basis of these broad diagnoses that major therapeutic decisions are made. Before a pathologist does a frozen section he should have all the clinical data. Frozen section diagnosis is not a game to see whether the pathologist can make a diagnosis without any history. This diagnosis is an important decision for a living patient on the operating table. At times the patient may have had previous surgery at some other institution and this material should be obtained and studied in advance by the pathologist. He should enter the operating room and look at the lesion in situ and at times he may be able to make suggestions as to where the biopsy should be taken. The pathologist must not make false positive diagnoses, for if a breast is removed on an incorrect frozen section diagnosis of cancer this unfortunate occurrence does not have to happen more than two or three times to invalidate completely the use of frozen section diagnosis in that hospital. The surgeon must have complete confidence in his pathologist, know that he is conservative, always conscious of the patient's welfare, and be certain in his mind that if the pathologist says it is cancer, it will prove to be so in almost one hundred per cent of the instances.

ERRORS IN FROZEN SECTION DIAGNOSIS

Certain generalizations can be made concerning errors in frozen section diagnosis. These errors will be reduced to a minimum if all clinical data are available to the pathologist and if the frozen section technique is of high quality. At times, unfortunately, the pathologist may allow himself to be swayed by apparently overwhelming clinical data. However, he must report only what he sees in the frozen section. Inflammatory cells trapped in dense connective tissue and scars, proliferating pseudo acini formed by mesothelium, endometrium within lymph-nodes, heterotopic pancreatic ducts coursing through muscle, and many other such lesions may be mistaken for cancer if the pathologist is not alert to these possibilities.

False negative reports are sometimes given under the following circumstances: material is submitted for frozen section and a piece or pieces of tissue are selected to freeze. It may be thought that this material is representative and frozen section will then be done and no significant pathologic findings observed. Later when all of the material is seen in the permanent sections, an area of previously unsuspected carcinoma or some other pathological abnormality will be found. This indicates how imperative it is that the material for the frozen section be selected with the greatest of care. Of course, if the material submitted is abundant, the number of frozen sections that can be done is only limited by time and there are practical limits to how many frozen sections can be done.

Of necessity an experienced pathologist must report his diagnosis, and usually this is not simply a report that it is cancer or not cancer, but it is a matter of discussion with the surgeon so that a decision may be reached for the best interests of the patient. Although it has been said that the pathologist must be conservative, he must not be so conservative that he never makes a decision. At times he may say that he is unable to make a diagnosis. But in practically all instances he must arrive at a decision, otherwise his value to the surgeon is tremendously diminished.

Because he is pushing his knowledge to the limits, he will, necessarily, make rare errors.

CLINICAL DATA

We have reviewed 1269 consecutive frozen sections on various organs in the time period 1952–55. As *Table I* indicates, 727 (57·3 per cent) of the total number of lesions were tumours, and of these 611 (84·1 per cent) were malignant and 116 (15·9 per cent) were benign. The remaining lesions, 542 (42·7 per cent), were non-neoplastic in nature. In most organs tumours were diagnosed in a high percentage of instances. For instance, of 440 frozen sections done on the breast 263 (59·3 per cent) were tumours and 205 (77·8 per cent) of these were malignant. In 143 frozen sections of lung 89 (62·2 per cent) were tumours, of which 84 (90·4 per cent) were cancers. Furthermore, the high percentage of tumours in the material submitted for frozen section can be appreciated in this *Table*. We had an overall accuracy of 98 per cent. We made 4 (0·3 per cent) false positive and 22 (1·7 per cent) false negative diagnoses.

Table I.—FROZEN SECTION DIAGNOSIS IN 1269 CASES

ORGAN	NO. OF FROZEN SECTIONS	FALSE POSITIVE	FALSE NEGATIVE	TUMOURS		
				Total	Malignant	Benign
Breast	440	0	4	263 (59·3 per cent)	205 (77·8 per cent)	58
Soft tissue	99	2	0	69 (69·7 per cent)	57 (57·6 per cent)	12
Thyroid	63	0	2	19 (30·2 per cent)	12 (19·0 per cent)	7
Prostate	21	0	3	10 (47·6 per cent)	10 (47·6 per cent)	0
Liver	42	0	0	26 (61·9 per cent)	25 (59·5 per cent)	1
Bowel	70	0	1	38 (54·3 per cent)	24 (34·3 per cent)	14
Lymph-nodes	143	0	3	63 (44·1 per cent)	63 (44·1 per cent)	0
Lung	143	2	1	89 (62·2 per cent)	84 (90·4 per cent)	5
Pancreas and peri-ampullary region	68	0	6	49 (72·1 per cent)	46 (67·6 per cent)	3
Stomach	58	0	1	24 (41·4 per cent)	18 (31·0 per cent)	6
Skin	35	0	1	22 (62·8 per cent)	22 (62·8 per cent)	0
Oral cavity	22	0	0	12 (54·5 per cent)	11 (50·0 per cent)	1
Miscellaneous	65	0	0	43 (66·1 per cent)	34 (52·3 per cent)	9
TOTAL	1269	4 (0·3 per cent)	22 (1·7 per cent)	727 (57·3 per cent)	611 (84·1 per cent)	116 (15·9 per cent)

Overall accuracy, 98 per cent; overall error, 2 per cent.

THE RISK OF IMPLANTATION

Implantation of tumour at the time of frozen section is a risk which varies tremendously with the organ. It is important that the surgeon realize that this is a distinct possibility and say to himself, first, is this frozen section necessary in order to define treatment? Certainly in the thyroid and in the lung we have already demonstrated the risk of implantation. Thyroid cancer can be implanted in the soft tissues of the neck if the tumour is incised or enucleated. Carcinoma of the lung can be implanted within the soft tissues or within the pleural cavity if the tumour is incised. In both of these instances excision of the tumour with a margin of normal tissue will completely avoid the risk. In the gastro-intestinal tract the risk is much greater and more difficult to avoid. In the stomach there is no reason to do frozen sections for ulcers except perhaps in those located high in the lesser curvature. In the latter case frozen section is indicated in spite of the risk of implantation, because if the lesion is benign conservative therapy is indicated, and if malignant total gastrectomy has to be done. If we have a debatable lesion in the cæcum, the problem is resolved in the following fashion: Let us assume that the radiologist makes the diagnosis of questionable carcinoma of the cæcum. At the time of exploratory laparotomy a pathologic abnormality within the cæcum is found but its exact nature cannot be determined. Under these circumstances we recommend ileocolectomy without frozen section, for even if the lesion turns out to be benign, the ileocolectomy in the hands of an experienced surgeon can be done without mortality and morbidity. Thus

we avoid the implantation of cancer. The risk of implantation in carcinoma of the pancreas is great; however, the curability in those cases is practically zero and the morbidity of a one-stage pancreatoduodenectomy is extremely high. Therefore, frozen section is well indicated.

If a tumour is highly undifferentiated and placed on a roughened vascular surface then it has a good chance of growing. For instance, a patient was

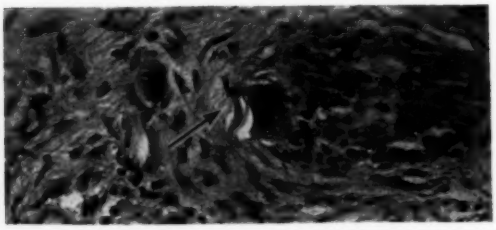

FIG. 363.—Photomicrograph of implanted cancer of the kidney in intimate association with suture material. Arrow identifies this suture material. W.U. Ill. No. 57-7208. (× 240.)

explored for an abdominal mass of unknown aetiology. Lymph-nodes in the region of the aorta were enlarged and frozen section demonstrated lymphosarcoma. A mass was palpated within an intact kidney. Biopsy was taken of this vascular mass and the peritoneum repaired. Frozen section showed cancer of the kidney. Three weeks later this kidney was removed and a section of a small nodule in the peritoneum was taken. This section showed implanted cancer of the kidney intimately associated with suture material. (*Fig.* 363.)

The operative situations reviewed are representative of the problem. Most surgeons realize that the risk is present and usually may be avoided by proper technique. This problem will be discussed further under the different organs.

FROZEN SECTION TECHNIQUE

The technique of frozen section is not difficult, but frozen sections must be thin, clearly stained, and performed in a short period of time. The method we use is not necessarily the best one, but it is one to which we have become accustomed. We use Hazard's method (Hazard and Stevenson, 1949). Dockerty's method (Dockerty, 1953) is equally effective in his experienced hands. We use a Sartorius microtome which can cut a section as thin as 7 μ and cuts each section the same thickness. We do not feel that the time-consuming H. and E. method is necessary and we prefer a rapid polychrome dye such as toluidine blue. This, of course, stains the tissues differentially and the method is as follows:—

A piece of tissue is removed from the fresh specimen and is placed in ten times its volume of fixative* and heated just at the boiling point over a burner. The tissue is frozen with freon and cut with a Sartorius microtome at 10–15 μ. The sections of tissues are stained with a 0·5 per cent solution of toluidine blue in 20 per cent alcohol for 10 sec. They are then washed in normal saline. They are counterstained with carbol-fuchsine for 5 sec. and washed again in normal saline. The sections are mounted on a slide (from the water) and covered with one to two drops of Brun's clearing fluid* and a cover slip.

Results: Nuclei—blue to purple; collagen—reddish; elastic tissue—red as it also stains differentially.

BREAST

In evaluating lesions of the breast the invariable decision is whether the lesion is benign or malignant. We performed 440 consecutive frozen sections on breast lesions, and *Table II* indicates that 263 (59·3 per cent) were tumours, of which 205 (77·8 per cent) were malignant and 58 (22·0 per cent) were benign. Carcinoma was diagnosed in 203 (99·0 per cent) instances. Fibro-adenomas accounted for the majority of the benign breast tumours. Chronic cystic disease was diagnosed 139 (31·6 per cent) times. We had no false positives in our series. We had 4 false negative diagnoses and in 10 instances the diagnosis was deferred.

On palpation of single dominant nodules the expert clinician has an accuracy of only 70 per cent and this indicates the necessity of exploring surgically such nodules. There are many conditions that can exactly mimic cancer and these include fat necrosis, duct ectasia with retraction of the nipple, sclerosing

Table II.—FROZEN SECTIONS OF BREAST

Type of Lesion	*No.*	*Per Cent*
Carcinoma	203	46·2
Other malignant lesions	2	0·5
Fibro-adenoma	51	11·6
Intraductal papilloma	6	1·4
Granular-cell myoblastoma	1	0·2
Chronic cystic disease	139	31·6
Acute and chronic inflammation, duct ectasia, and fat necrosis	18	4·1
Other benign lesions	20	4·5
TOTAL	440	100·0

False positives, 0; false negatives, 4; deferred, 10.

adenosis, and the rare lesion granular-cell myoblastoma. Furthermore, malignant conditions can mimic benign conditions and we have seen movable circumscribed masses thought to be fibro-adenoma turn out to be carcinoma. If we have a lesion 2·5 cm. or less we recommend that it be excised, for carcinoma could be missed in such lesions if an incisional biopsy is done. On the other hand, if the lesion is a large one, probably carcinoma, then we feel it is better to do an incisional biopsy rather than excise the entire tumour. If the lesion is excised then there is trauma to the tumour and to surrounding breast parenchyma, with possible opening of venous and lymphatic channels with increased chances of dissemination of the cancer. Therefore, with a large tumour mass we do a careful incisional biopsy.

In lesions of the breast submitted for frozen section we either tell the surgeon that it is cancer, not cancer, or that we do not know. As can be seen from *Table II*, it is relatively rare for us to delay our

* An acetic-alcohol-formalin fixative is used and it has the following composition:

Formalin 1:10	70 ml.
Ethyl alcohol (95 per cent)	29 ml.
Glacial acetic acid	1 ml.

* Brun's clearing fluid:

Glucose (Bacto-Dextrose)	24 g.
Glycerin	6 c.c.
Spirits of camphor	6 c.c.
Distilled water	84 c.c.

diagnosis, and it is true that in most instances when we delay the diagnosis it will turn out to be carcinoma. We delayed our diagnosis in 10 instances and the lesions turned out to be cancer in 8. The greatest difficulty is encountered in papillary and intraductal lesions. Intraductal papillomas are particularly difficult and it is not unusual for inexperienced pathologists to call such lesions cancer. This statement is not surprising, for in the older literature good photomicrographs of intraductal papillomas are captioned as grade 1 cancers. These errors can be avoided if attention is given to the gross specimen and if an adequate frozen section preparation is done.

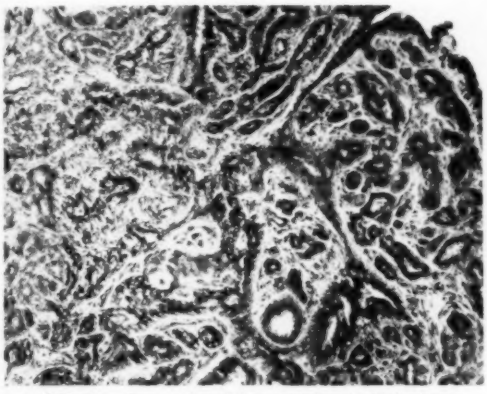

FIG. 364.—*Case* 1. Actual frozen section of cellular intraductal papilloma. Note absence of necrosis and good supporting stroma. W.U. Ill. No. 57-501. (× 84.)

Case 1.—Mrs. L. M., a 35-year-old white female, was admitted to Barnes Hospital with a history of discharge from the right nipple, at first cloudy and in the last six months bloody in character, associated with a small, painless lump in the breast located beneath the areola. At operation a 4-cm. mass of breast parenchyma was excised and submitted for frozen section. Careful examination of the gross demonstrated a dilated duct with a small papillomatous mass within it. On frozen section (*Fig.* 364) the lesion was diagnosed as intraductal papilloma. This lesion was highly cellular, but individual glands were well supported by connective tissue and the clinical history and gross examination supported the diagnosis of intraductal papilloma.

In intraductal cancer (so-called 'comedo carcinoma') the tumour is confined to the ducts and therefore the diagnosis of cancer has to be made on cytologic abnormalities. This can usually be done by doing both thin and thick sections. Thick frozen sections will demonstrate the pattern of the tumour and will prevent the masses of cells from falling off the ducts. Thin sections will be more adequate for the study of cellular detail. Sclerosing adenosis is also difficult to interpret because of the apparent invasion of the surrounding tissues. The gross specimen may even show apparent chalky streaks. On microscopical examination the diagnosis is best made by paying attention to lobulation, lack of necrosis, and well-differentiated glands. As in all other lesions, it is imperative that the pathologist have a conservative attitude in the interpretation of the frozen section.

Case 2.—A 32-year-old coloured female gave a history of lumps in both breasts of six years' duration. These lumps became enlarged and painful just before the menstrual periods. There were no other significant findings and radiographic studies were negative for evidence of metastatic disease. The patient was operated upon and lesions from both breasts were submitted for frozen section. Frozen section diagnosis was 'sclerosing adenosis' (*Fig.* 365). Grossly both specimens consisted of well-delimited, non-encapsulated nodules measuring 1·5 × 1 × 1 cm. The lesion microscopically under low power shows well-defined lobulation with good supporting connective-tissue framework and absence of necrosis. Under high magnification the individual cells are uniform.

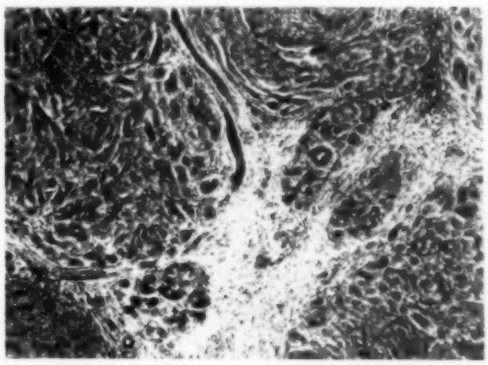

FIG. 365.—*Case* 2. Actual frozen section of sclerosing adenoma of breast with rather sharply demarcated lobules with excellent supporting connective-tissue framework. W.U. Ill. No. 57-4494. (× 27·5.)

This lesion is confused with cancer because of the extreme cellularity and apparent invasion of connective tissue. The difficulties of diagnosing it have been well described by Urban and Adair (1949) and Dawson (1954).

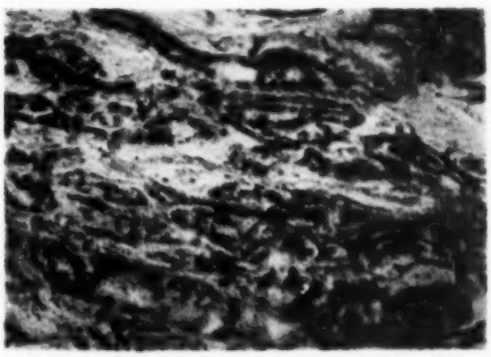

FIG. 366.—*Case* 3. Actual frozen section of classic adenocarcinoma of the breast. W.U. Ill. No. 56-4998. (× 125.)

Diagnosis of the usual cancer of the breast can be made from gross examination. The diagnosis clinically, if the lesion is advanced, is usually not difficult. However, in our institution radical mastectomy is not done without confirming the diagnosis. We have seen clinical examples of lesions

that have exactly mimicked cancer—such as fat necrosis, granular-cell myoblastoma, duct ectasia with inflammation, and even lipoma. The following case is representative:—

Case 3.—Mrs. M. M., a 46-year-old white female, discovered a lump in her left breast six weeks prior to admission to this hospital. This nodule had increased in size during that period. There was no nipple discharge or bleeding. Physical examination was negative except for a

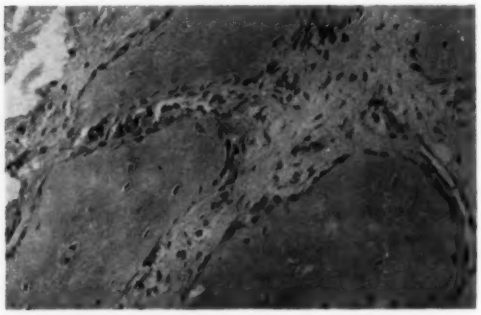

FIG. 367.—*Case* 4. Photomicrograph of well-demarcated bone trabeculæ, separated by rather vascular connective-tissue background. Classic example of myositis ossificans. W.U. Ill. No. 57-2122. (× 137·5.)

4-cm. firm, slightly tender mass in the upper outer quadrant of her left breast. There was no fixation to the skin or pectoral fascia. Radiographic studies were negative for evidence of metastatic disease. An incisional biopsy and frozen section were done. Frozen section diagnosis was carcinoma (*Fig.* 366). Therefore, a radical mastectomy was done.

Comment.—This lesion was diagnosed clinically as carcinoma and a definite diagnosis on frozen section enabled the surgeon to do definitive therapy at the time of operation. As we have mentioned before, in lesions of the breast 2·5 cm. or larger, we do an incisional biopsy with frozen section. We feel that the chances of dissemination of tumour are decreased with incisional biopsy rather than trying to excise the entire tumour. As can be seen in *Fig.* 365, diagnosis of carcinoma of the breast on frozen section is not difficult in most instances.

SOFT-TISSUE TUMOURS

There are innumerable lesions, neoplastic and non-neoplastic, that can occur in the soft tissues (*Table III*). In 99 frozen sections of soft-tissue lesions a tumour was diagnosed in 69 (69·6 per cent)

Table III.—FROZEN SECTIONS OF SOFT TISSUE

Types of Lesion	*No.*	*Per Cent*
Carcinoma	38	38·4
Sarcoma	15	15·1
Miscellaneous malignant tumours	4	4·0
Benign tumours	12	12·1
Myositis ossificans	1	1·0
Sympathetic chain	4	4·0
Chronic inflammatory processes	18	18·1
Other lesions	7	7·1
TOTAL	99	100

False positives, 2; false negatives, 0.
Tumours, 69·7 (malignant, 57·6; benign, 12·1).

instances. Fifty-seven (82·6 per cent) of these tumours were malignant. In 38 (66·6 per cent) instances the diagnosis was carcinoma, either invasive or metastatic from a primary elsewhere. Fifteen primary sarcomas of soft tissues were diagnosed in this series. There were 12 benign tumours and in 30 instances the lesion was non-neoplastic. We made 2 false positive and no false negative diagnoses. In one instance the bizarre fat cells, benign in nature, were thought to be neoplastic and, in the other, prominent fibrous-tissue proliferation caused difficulty. In neither instance was

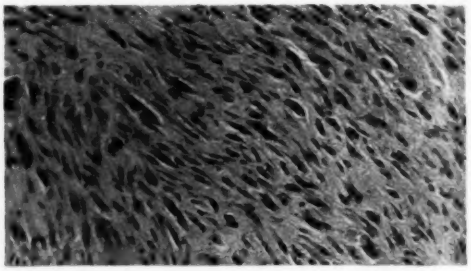

FIG. 368.—*Case* 5. Photomicrograph of fairly well-differentiated fibrosarcoma of soft tissue of popliteal area. W.U. Ill. No. 57-4884. (× 137·5.)

anything but conservative surgery done. In several instances of a soft-tissue mass of questionable malignant nature the problem was resolved by the frozen section and conservative surgery was done. The following is an example:—

Case 4.—Mr. O. McC., a 35-year-old white male, noted a mass in the volar aspect of the left forearm and consulted a physician after a four-months' time period. The firm, non-tender lesion measured 6 × 4 cm. and was not attached to the skin. It was apparently rather superficial. The regional axillary lymph-nodes were not enlarged. The clinical diagnosis was sarcoma. An incisional biopsy of this firm mass was done and frozen section showed myositis ossificans (*Fig.* 367). Therefore, conservative, local excision was performed.

In the soft-tissue sarcoma group there are numerous instances where the surgeon does a formal incisional biopsy, does not request a frozen section, and waits for the report of the permanent sections. We are perfectly willing to attempt frozen section diagnosis in soft-tissue sarcomas. The therapeutic decision implied may indicate major surgery and if there is any doubt we ask the surgeon to wait for the permanent sections. However, as the following case indicates, frozen section is extremely valuable in determining the nature of soft-tissue masses.

Case 5.—Mr. N. K., a 65-year-old white male, entered Barnes Hospital for the first time because of a tumour in the right leg of two months' duration. The tumour was located in the popliteal space and it was firm, fixed to the underlying structures but not to the skin. The popliteal pulse was not palpable and there was œdema of the lower extremity. Radiographs revealed a soft-tissue mass without evidence of bone involvement. Chest film was negative for evidence of metastases. An incisional biopsy with frozen section was done. Frozen section diagnosis was 'fibrosarcoma' (*Fig.* 368). Therefore, a midthigh amputation was performed on the basis of our frozen section diagnosis. Examination of the amputated leg showed a tumour surrounding the popliteal artery and vein. The tumour was 5 × 6 cm. in size. Microscopical examination of the permanent paraffin sections confirmed our diagnosis.

Comment.—We feel that this patient was treated correctly under the circumstances. This was a rapidly growing tumour fixed to the underlying structures and surrounding the popliteal artery and vein. The diagnosis of fibrosarcoma on frozen section enabled the surgeon to do the only operation that was indicated, a midthigh amputation, as the tumour could not be adequately resected locally and the definitive operation was not delayed. On the other hand, if no frozen section had been done the surgeon may have been tempted locally to excise the tumour and this would have compromised further definitive surgery.

We must stress the fact that, if a patient has a soft-tissue tumour that is not obviously a lipoma, this tumour should not be enucleated, for the encapsulation

Table IV.—CLINICAL EVALUATION OF PRELIMINARY BIOPSY

	No. of Cases	*Local Recurrences*
Without biopsy	27	21 (78·8 per cent)
With biopsy	12	2 (16·6 per cent)
TOTALS	39	23 (59·9 per cent)

present is false and tumour may be implanted over a wide area. This, of course, may prejudice later adequate and definitive surgery. We feel that incisional biopsy should be done and adequate excision be planned according to the nature of the tumour and its anatomical location. Proof of this thesis is shown in *Table IV*, which indicates the high local recrudescence rate in primary treatment without biopsy, in contrast to the low rate following biopsy and adequate excision (Lieberman and Ackerman, 1954).

THYROID

Frozen section diagnosis in lesions of the thyroid is often considered too difficult to attempt. We are convinced that a definitive diagnosis is possible in a high percentage of instances and in practically all cases the decision that has to be made is whether the patient has or does not have cancer.

At the time of surgical exploration, if the tumour has extended beyond the capsule to the soft tissues, muscle, or involves the regional lymph-nodes, the solution is simple, for the biopsy will show obvious carcinoma. If a pathological process involves the entire thyroid gland and has not extended beyond the capsule, then common sense dictates that this cannot be cancer, for if it were it would have extended beyond the capsule. Biopsies in such instances usually show thyroiditis or Hashimoto's disease. The major problem confronting the surgeon is the patient with a single dominant nodule within the substance of the thyroid. Clinically it is impossible for even the most astute clinician to determine the nature of such nodules on physical examination. Unfortunately, in the past such nodules were enucleated and if they were cancer, tumour was often successfully implanted in the tissues in the region of the thyroid. We insist that if a patient has a single nodule then it must be excised with a margin of normal thyroid and in most instances this implies lobectomy. In our 12 cases of cancer in this series only 7 were suspected clinically.

At the time of frozen section in a euthyroid patient the microscopical diagnosis of undifferentiated cancer or other forms of cancer, with the exception of the follicular type, is not difficult. In our series of 63 patients a tumour was diagnosed in 19 (30·2 per cent) instances (*Table V*), and of these 12 (63·2 per cent) were primary thyroid cancers and 7 (36·8 per cent) were adenomas. There were only 2 false negative diagnoses. One of these was a papillary carcinoma which was well differentiated and the psammoma bodies that were present were not given the importance that they deserved so that an accurate diagnosis could not be made. In 5 of the 12 cases of cancer the lesion was thought to be benign clinically and proven to be cancer on frozen section. Furthermore, cancer was suspected clinically in 3 instances in the non-neoplastic group and these were diagnosed on frozen section as thyroiditis, Hashimoto's disease, and nodular goitre. In our group of cases there were no false positive diagnoses.

Errors have been made in the frozen section diagnosis of thyroid lesions under certain circumstances. It must be constantly remembered that during the development of the thyroid gland small remnants of thyroid may become completely separated from the thyroid proper. Since thyroid remnants may show the same pathological processes that occur in the thyroid gland proper—such as hyperplasia, nodular goitre, and lymphadenoid goitre—the finding

Table V.—FROZEN SECTION OF THYROID

Type of Lesion	*No.*	*Per Cent*
Multiple nodular goitre	30	48
Carcinoma (Papillary 6, others 6)	12	19
Adenoma	7	11
Other lesions	14	22
TOTAL	63	100

False positives, 0; false negatives, 2.

of such a nodule at the time of operation in the immediate vicinity of the thyroid may lead the inexperienced surgeon to believe that he is dealing with metastatic cancer. Such nodules may also extend into the mediastinum and be in other rare locations, such as in the posterior mediastinum. The extension of thyroid tissue into muscle used to be considered a clear-cut indication that thyroid cancer was present. Invasion of muscle of non-neoplastic nature can occur under certain circumstances. As Meissner (Warren and Meissner, 1953) has pointed out, in an extreme degree of hyperplasia hyperplastic thyroid tissue may directly invade the adjacent skeletal muscle and this may be mistaken for cancer. The recognition of this is not difficult because the clinical signs and symptoms will alert the pathologist and under these circumstances frozen sections are usually not requested. If the patient has had previous surgery, thyroid tissue—non-neoplastic—may be implanted within the substance of the muscle and if a second operation is performed these findings may be thought to be cancer. The history of previous operation, the microscopical pattern of the tissue, and the presence of suture material are helpful in eliminating cancer. Finally, in certain bizarre conditions in children a pathologic process difficult to diagnose will

extend to within the muscle-bundles. Gardiner (1956) has commented on this fact and has described skeletal muscle-fibres within the thyroid gland as well as intramuscular thyroid follicles within the thyrohyoid and sternohyoid muscles. Embryologically continuity once existed between the thyroid and the primitive pharynx and these findings are related to the persistence and subsequent intermingling of glandular and muscle elements as the developing thyroid gland and muscle anlagen shift caudally and cranially respectively.

In the presence of a thyroid nodule of unknown nature a decision can invariably be made at the operating table whether further definitive surgery is indicated and if needed it can be done at the time of

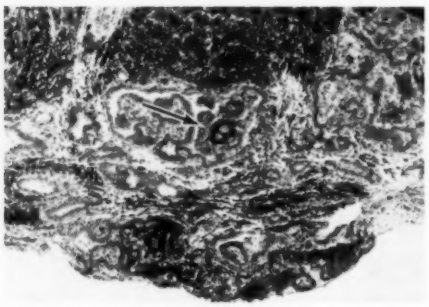

FIG. 369.—*Case* 6. Actual frozen section of small lymph-node demonstrating papillary adenocarcinoma. Note psammoma body at arrow. Such psammoma bodies are diagnostic of papillary cancer of the thyroid. W.U. Ill. No. 57-500. (× 70.)

operation. In our experience thyroid cancer is not a rare disease and, therefore, we believe that thyroid nodules should be surgically explored (Underwood, Ackerman, and Eckert, 1958). The incidence of carcinoma in asymptomatic nodules of the thyroid ranges from 4 to 50 per cent (Morfit and Reimers, 1956), and, therefore, the only reason for operating on patients with thyroid nodules is to determine whether the lesion is benign or malignant. We have found frozen section extremely useful in evaluating these nodules and in many instances radical surgery was performed on the basis of our frozen section diagnosis. The following case illustrates the value of frozen section in evaluating thyroid lesions:

Case 6.—Mrs. E. B., a 30-year-old white female, was admitted to this hospital for the delivery of her fourth child. During a routine physical examination, a firm nodule was discovered in the right lobe of the thyroid. There were also several small palpable lymph-nodes in the right side of the neck. The thyroid nodule had been present for one year and there had been slight increase in its size in the past four months. Radiographs of the chest and skeletal system were negative for evidence of metastatic disease. The patient was explored three weeks after delivery and a 4-mm. cervical lymph-node was excised and submitted for frozen section. The node contained metastatic papillary carcinoma from the thyroid (*Fig.* 369). A right hemithyroidectomy and right radical neck dissection in continuity was done on the basis of our frozen section diagnosis. The gross specimen presented a 2·5 × 2 cm. firm, non-encapsulated tumour in the upper pole of the right lobe of the thyroid (*Fig.* 370). Permanent paraffin sections showed papillary adenocarcinoma of the thyroid with metastases to 8 of 56 regional lymph-nodes.

Comment.—We believe this case was handled correctly and adequate surgery done. If no frozen section had been done, then a second operation would have been necessary, with increased chances of disseminating cancer and compromising perhaps future definitive surgery. Also a better radical neck dissection can be done by removing the thyroid and the lymph-node bearing tissues of the neck as part of the same operative procedure.

PROSTATE

There has been a resurgence in the operation of perineal prostatectomy for cancer, and under the

FIG. 370.—*Case* 6. Gross photograph of papillary cancer of the thyroid. This was the primary tumour which produced the metastases seen in *Fig.* 369. W.U. Ill. No. 57-541.

stimulation of men like Hudson (Hudson, Finkle, Hopkins, Sproul, and Stout, 1954) more patients with suspicious nodules of this organ are being explored with frozen section diagnosis and radical perineal prostatectomy performed if the frozen section demonstrates cancer. In the early cases of carcinoma of the prostate transurethral removal of prostatic tissue is invariably negative. It is often difficult to be accurate with a needle biopsy. However, if a needle biopsy is positive this obviates the need for frozen section. For an open perineal biopsy, we recommend that the exposure be the one used by Hudson (Hudson, Finkle, Hopkins, and others, 1954), for under such circumstances a complete representative section of the prostate can be obtained, particularly of the posterior lobe. A biopsy of the prostate is performed through a perianal incision and a rectangular wedge of prostatic tissue 1 cm. in width and as long as the widest portion of the prostate gland is removed. It extends in depth into the peri-urethral glandular tissue and the tissue is obtained with the scalpel. This specimen will include a good portion of the anatomical capsule of the prostate. Such a biopsy specimen is adequate and this is important, for the hard area felt on digital examination may not be cancer but can be localized proliferation of smooth muscle, a stone, an infarct, or even granulomatous prostatitis. The soft area next to the hard one may even be a cellular malignant tumour, for a fair percentage of prostatic cancers are highly cellular, with little stroma, and are therefore soft in consistency. In early prostatic cancer induration is perhaps the exception rather than the rule.

During the last few years we have been doing more frozen sections, but we still feel that this method has not been fully exploited at our institution. In our series (*Table VI*) we performed 21 frozen sections on prostatic lesions and in 10 (47·6 per cent) instances the lesion was cancer. Cancer was clinically suspected in 8 of the 10 cases of carcinoma.

We missed 3 carcinomas on frozen section diagnosis. One of these was an extremely well-differentiated carcinoma without nerve-sheath invasion. More attention should be paid to the pattern

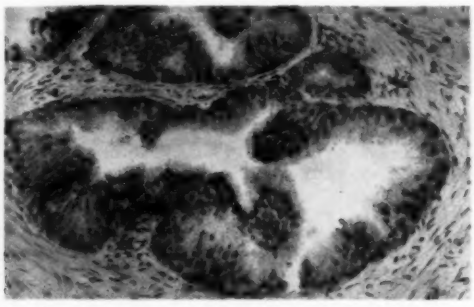

FIG. 371.—*Case* 7. Actual frozen section of a benign lesion of the prostate with normal appearing gland. W.U. Ill. No. 57-422. (× 125.)

of the neoplasm and the single layer of cells lining the acini. Totten (Totten, Heinemann, Hudson, Sproul, and Stout, 1953) has emphasized the atypical nature of cells lining the acini and the single layer of cells as contrasted to a double layer in non-cancerous lesions. In the second false negative the only evidence of cancer was a small area of nerve-sheath invasion which we missed. In the third false negative we did three frozen sections without evidence of cancer and

Table VI.—FROZEN SECTIONS OF PROSTATE

Type of Lesion	*No.*	*Per Cent*
Adenocarcinoma	10	48
Nodular hypertrophy	7	33
Other lesions	4	19
TOTAL	21	100

False positives, 0; false negatives, 3.

no tumour was found in the permanent sections of the material used for frozen section. Cancer was found in other material submitted to us which unfortunately was not frozen. Cancer was also suspected clinically in 4 of the non-neoplastic cases. We made no false positive diagnoses in our series. The non-neoplastic cases represent, for the most part, adenomatous hyperplasia of the prostate, tuberculosis, granulomatous prostatitis, areas of infarction, areas of fibrosis, and squamous-cell metaplasia. All may be difficult to recognize as non-malignant, either grossly or microscopically.

Case 7.—A 64-year-old white male entered the hospital because of urinary symptoms, and on physical examination the prostate was found to be enlarged and in one area in the left lateral lobe there was a firm nodule clinically suspicious of carcinoma. Radiographic studies and alkaline and acid phosphatase levels were normal. An open perineal biopsy with frozen section was done. Frozen section diagnosis was 'nodular hyperplasia' (*Fig.* 371). The prostate was enucleated, therefore, and the permanent paraffin sections confirmed our frozen section diagnosis.

The following case demonstrates the value of frozen section in determining the nature of another prostatic lesion very similar to the first case:

Case 8.—L. D., a 55-year-old white male, was admitted to Barnes Hospital for evaluation of a prostatic nodule. A

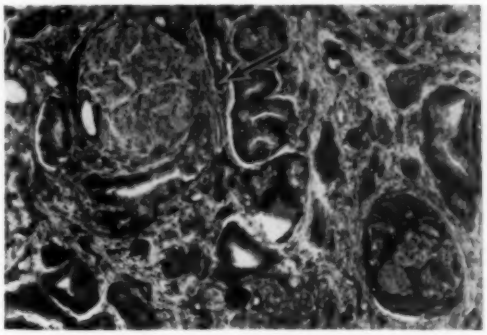

FIG. 372.—*Case* 8. Actual frozen section showing nerve-sheath invasion at the arrow. This is pathognomonic of cancer of the prostate. W.U. Ill. No. 57-2132. (× 120.)

firm dominant nodule was palpable in the right lateral lobe. The levels of alkaline and acid phosphatase were normal and radiographic studies of the chest and skeletal system did not show evidence of metastases. An open perineal biopsy with frozen section was done and the diagnosis of adenocarcinoma of the prostate was made (*Fig.* 372). Therefore, a radical perineal prostatectomy was performed on the basis of our frozen section diagnosis. The prostate gland weighed 45 g., and on cut section there was a yellow nodule 2 cm. in diameter in the right lateral lobe also involving the posterior lobe. Permanent paraffin sections showed adenocarcinoma with nerve-sheath invasion. There was also extension into the seminal vesicles.

Comment.—In this case carcinoma was suspected clinically and an open perineal biopsy with frozen section enabled the urologist definitely to establish the diagnosis of cancer and to proceed with a radical operation in a relatively early case. We believe that by using this method more cases of cancer confined to the prostate will be discovered, thereby increasing chances of cure by radical perineal prostatectomy.

A recent article from the Mayo Clinic by Culp and McDonald (1953) demonstrates how accurate frozen section can be. In 45 cases there were no false positive diagnoses and all 40 cases of cancer were identified on frozen section. All 40 cases of cancer were treated by radical perineal prostatectomy on the basis of frozen section diagnosis.

LIVER

Surgeons frequently explore the abdomen and with an obvious pre-operative diagnosis of carcinoma of the stomach or large bowel find that there are nodules in the liver. The clinical impression has invariably been that such nodules represent metastatic cancer, but, as has been shown by many, there are many nodules in the liver that are not cancer. These

may be fibrous nodules, adenomas of bile-ducts, healed tubercles, lymphangiomas, hæmangiomas, and so forth.

Case 9.—The patient, a 20-year-old girl, had a carcinoma of the ureter and on abdominal exploration there were three large nodules in the liver between 3 and 4 cm. in diameter, firm, greyish-white, and slightly

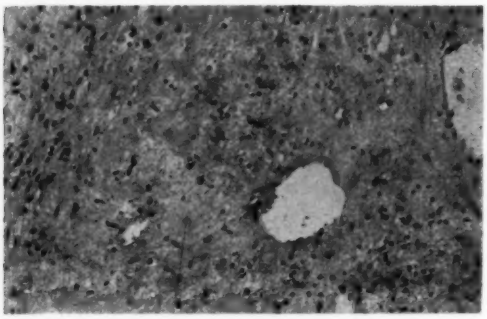

FIG. 373.—*Case* 9. Photomicrograph of the liver demonstrating focal fibrosis. This lesion was mistaken grossly for metastatic cancer. W.U. Ill. No. 57-7206. (× 145.)

depressed. The clinical impression of an extremely experienced surgeon was carcinoma. Biopsy and frozen section demonstrated merely focal fibrosis without tumour (*Fig.* 373).

If a nodule in the liver proves to be cancer on frozen section then this may modify to a large extent the surgery contemplated in a case of carcinoma of the stomach or large bowel. Furthermore, if a lesion in the liver proves to be benign such finding will encourage the surgeon to do a definitive cancer operation. In some instances nodules in the liver are so located that they are not accessible to the usual biopsy and therefore a Silverman needle biopsy

Table VII.—FROZEN SECTIONS OF LIVER

Type of Lesion	*No.*	*Per Cent*
Carcinoma	25	60
Cirrhosis	5	12
Hæmangioma	1	2
Bile-ducts present	4	9
No bile-ducts present	1	2
Other lesions	6	14
TOTAL	42	99

False positives, 0; false negatives, 0.

through an intercostal space under visual guidance by the surgeon can be done. The material obtained can be used for frozen section and we have had little difficulty with the preparation and interpretation of this type of biopsy. Extensive metastases in the liver as proven by frozen section may completely negate any thought of surgery.

In children in whom there is a congenital absence of the extra-hepatic bile-ducts, frozen sections have been done to determine the presence or absence of bile-ducts in the liver. Such frozen sections have been done in the hope that an occasional case might have large enough ducts to anastomose directly to small bowel. Unfortunately in the past five years we have not found a single patient with ducts large enough to contemplate anastomosis.

In our series we did 42 frozen sections on lesions of the liver (*Table VII*). In 25 (60 per cent) instances the lesion was metastatic carcinoma from a primary lesion elsewhere. Cirrhosis was diagnosed in 5 (12 per cent) instances. As can be seen by our figures, the usual problem is to determine whether a lesion is malignant or not. We made no false positive and no false negative diagnoses in our series.

SMALL AND LARGE BOWEL

Frozen section diagnosis of intraluminal and intramural lesions of the bowel are rarely indicated. Naturally if a lesion is within reach of the proctoscope a biopsy can be taken. In 2 instances intramural lesions of the bowel wall without mucosal lesion were thought to be carcinoma but proved on frozen section

Table VIII.—FROZEN SECTIONS OF SMALL AND LARGE BOWEL

Type of Lesion	*No.*	*Per Cent*
Carcinoma	24	34·3
Adenomatous polyp	12	17·1
Leiomyoma	2	2·9
Diverticulitis	3	4·3
Endometriosis	2	2·9
Other lesions	27	38·5
TOTAL	70	100

False positives, 0; false negatives, 1.

to be endometriosis. This diagnosis is easily made when typical endometrial glands are associated with typical endometrial stroma. The stroma is the important point in the diagnosis. In a single instance a patient with a proven carcinoma of the rectosigmoid was considered by the surgeon to have innumerable metastases in the immediate area of the tumour. These clinical metastases proved to be endometriosis on frozen section (*Table VIII*).

If a patient has a single adenomatous polyp on a stalk demonstrated radiographically, it is our policy in some instances to recommend a colotomy and remove the polyp with an ellipse of normal mucosa and submucosa. Frozen section of the stalk is the only frozen section indicated, for if the stalk is free of carcinoma then the patient, in our experience, will never have any further difficulty. We have yet to see an instance of carcinoma in an adenomatous polyp with metastases if the stalk is free of tumour. In sessile lesions or in debatable lesions of the cæcal area when the wall is involved but the nature of the process is uncertain, we feel that colotomy is not indicated because of the danger of implantation if the lesion proves to be carcinoma. Because of this policy, ileocolectomy has been done for appendiceal abscess with a defect in the cæcum, for localized diverticulitis in the cæcum, and for a large lipoma of the cæcal region. We do not feel that these are errors in judgement. In another institution we have seen a patient in whom a colotomy was done for a sessile polyp. The permanent sections demonstrated there was focal carcinoma near the base. Fifteen days later a local resection of this segment of bowel was done and there was no tumour found in the bowel or regional lymph-nodes but tumour was present in association with suture material near the bowel. This finding clearly indicates the chances of implantation.

We have also found frozen section to be of great value in cases of megacolon. At operation there is invariably an area of constriction proximal to the dilated colon. We feel that the only adequate method of determining at what level the resection should be done is by doing frozen section and looking for the presence or absence of ganglion cells. Before doing frozen sections for megacolon we did frozen sections

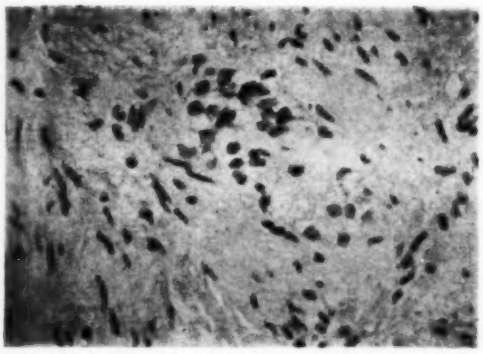

FIG. 374.—*Case* 10. Colour photomicrograph of an actual frozen section of a patient suspected of megacolon (Hirschsprung's disease). Ganglion cells are present in the constricted zone, therefore the patient did not have megacolon. W.U. Ill. No. 57-4886. (× 310.)

in normal bowel and we found that with a single section ganglion cells were present in 100 per cent of the cases. Therefore, on frozen section the presence or absence of ganglion cells is a highly reliable finding in determining therapy.

Case 10.—A 4-months-old white child was admitted to this hospital because of progressive vomiting, diarrhœa, and abdominal distension. The stools were described as loose, watery, yellow, and foul-smelling. The abdomen was markedly distended and on rectal examination the rectum was felt to be dilated. Barium enema studies were interpreted as being compatible with megacolon (Hirschsprung's disease). There was also evidence of mechanical obstruction. The child was operated upon and the colon was found to be of essentially normal calibre. No area of constriction of the colon could be identified at operation. The rectum was biopsied 4 cm. proximal to the anorectal line and the material was submitted for frozen section. Ganglion cells were identified on frozen section (*Fig.* 374). Permanent paraffin sections of the material submitted for frozen section confirmed the diagnosis. No operation was indicated and therefore no resection was done.

LYMPH-NODES

Frozen section diagnosis of lymph-nodes is reputed to be extremely difficult. If certain principles are considered the frozen section diagnosis of lymph-nodes is of great practical value. In this series we performed 143 frozen sections and we made 2 false negative and no false positive diagnoses (*Table IX*). In doing frozen sections in a lymph-node the gross is helpful in evaluating the pathology. The size and consistency is of little help. We have seen a 9-cm. lymph-node which was hyperplastic and we have also seen 3-mm. lymph-nodes which contained cancer. On cut section if the node is firm and grey, it is often not remarkable microscopically. If it contains areas of necrosis or if the node is partially replaced by some pathological process such changes are readily apparent. Of course, these changes may be due to granulomas or metastatic cancer. The fish-flesh appearance of lymphosarcoma is well known.

In 12 instances in our series we diagnosed lymphoma without difficulty. In these cases the problem was usually whether a node contained

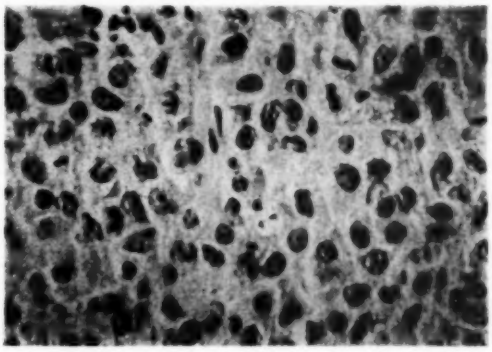

FIG. 375.—*Case* 11. Actual frozen section demonstrating undifferentiated epidermoid carcinoma within a lymph-node. W.U. Ill. No. 57-4885. (× 350.)

metastatic cancer or not. We are able to say that it is not metastatic cancer but lymphoma. It does not matter whether we make an exact diagnosis of the type of lymphoma, for once the patient has been placed in this category the case usually becomes a radiotherapeutic problem. In 51 (36 per cent) instances we made the diagnosis of metastatic carcinoma. Hyperplasia was diagnosed in 24 (17 per cent) instances and in 47 (33 per cent) there were no abnormal findings. Usually the diagnosis of carcinoma within a lymph-node is extremely easy and often lymph-nodes submitted are in patients with known cancers. If a lymph-node submitted contains metastatic cancer then the operation may be modified

Table IX.—FROZEN SECTIONS OF LYMPH-NODES

Type of Lesion	*No.*	*Per Cent*
Carcinoma	51	36
Lymphosarcoma	6	4
Hodgkin's disease	6	4
Hyperplasia	24	17
Other lesions	9	6
No abnormal findings	47	33
TOTAL	143	100

False positives, 0; false negatives, 3.

or even abandoned. In patients with persistent carcinoma of the cervix in whom pelvic evisceration is contemplated if a lymph-node along the aorta contains cancer, to our surgeons this finding indicates that the pelvic evisceration is not indicated. It is imperative that such frozen sections be done because palpation of a lymph-node as to whether it does or does not contain cancer is notoriously difficult to evaluate. The following 2 cases illustrate the value of frozen section under these conditions:—

Case 11.—A 42-year-old white female had a biopsy of the cervix at another hospital and a diagnosis of epidermoid carcinoma was made. She received irradiation

therapy and had severe back pain from that time on. The patient was referred to this hospital for further therapy and for biopsy of the cervix, which demonstrated persistent cancer. It was felt that the patient was a candidate for pelvic evisceration. The patient was taken to surgery and a lymph-node along the aorta was submitted for frozen section. Frozen section diagnosis was 'metastatic epidermoid carcinoma' (*Fig.* 375). The operation was abandoned, therefore, on the basis of our frozen section

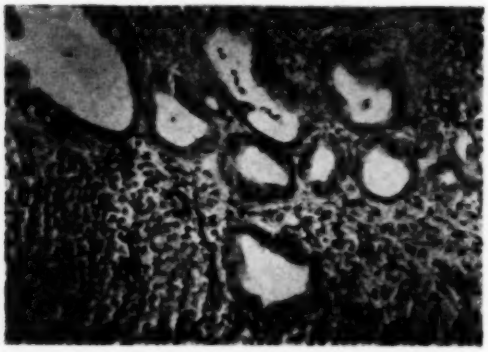

FIG. 376.—*Case* 12. Actual frozen section of endometrial tissue within a lymph-node. W.U. Ill. No. 57-4890. (× 130.)

diagnosis. If no frozen section had been done, unnecessary radical surgery might have been carried out.

Case 12.—A 37-year-old white female had a biopsy of the cervix which was diagnosed as carcinoma-in-situ, for which she was treated with irradiation. Subsequently she developed right lower quadrant pain and the question arose as to whether the patient had pelvic inflammatory disease or persistent cancer in the pelvis. She was explored with the thought of doing a pelvic evisceration if the process were cancer. At laparotomy the findings suggested an inflammatory process rather than cancer. Regional lymph-nodes were enlarged and one pelvic lymph-node was submitted for frozen section. The lymph-node showed hyperplasia and endometriosis (*Fig.* 376). Therefore, no further treatment was done.

LUNG

Because of the increased frequency of carcinoma of the lung, and because mass radiographic screening surveys are more frequently done, patients with debatable lesions are being referred in increasing numbers to surgeons in thoracic surgery centres. In the past bronchoscopic biopsy was positive in as high as 75 per cent of the patients with carcinoma of the lung who entered thoracic surgery clinics, but many of these patients had advanced pulmonary cancer. In clinics to-day patients suitable for surgery have a bronchoscopic study, but at the present time the bronchoscopic biopsy is positive in only 30 per cent of the resectable cases. Exfoliative cytology will increase the percentage to as high as 65 to 75 per cent of the total group. The smaller the peripheral lesion, the smaller is the chance that cytology will be positive. In 48 instances in our last series there were patients who had radiographic findings and a positive cytology, and in this group pneumonectomy or lobectomy was done without the benefit of frozen section (Spjut, Fier, and Ackerman, 1955). All of these patients proved to have cancer. In the remaining patients if there was a peripheral lesion in which the diagnosis was unknown we recommended excision of the nodule with a margin of normal lung parenchyma. In some instances lobectomy may even have to be done. Frozen section is then carried out. Incisional biopsy carries the risk of implantation on the pleural surface if the lesion proves to be cancer. In a recent case in which the lesion was close to the hilus an incisional biopsy was done and tumour spilled. This

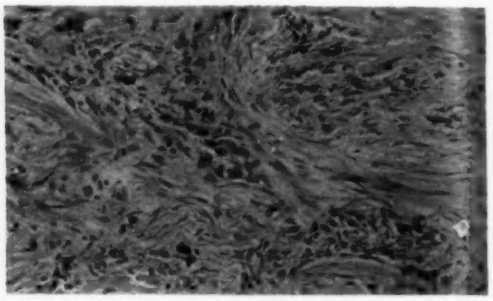

FIG. 377.—*Case* 13. Photomicrograph of the paraffin section demonstrating inflammatory cells present between fibrous muscle-bundles. These cells were mistaken at the time of frozen section for carcinoma. W.U. Ill. No. 57-854. (× 155.)

was proven because the pleural cavity was washed out with saline and the fluid studied contained large collections of obvious cancer cells.

In a review of our cases there was a high rate of accuracy. As *Table X* indicates, we did frozen sections in 143 consecutive cases. Cancer was

Table X.—FROZEN SECTIONS OF LUNG

Type of Lesion	*No.*	*Per Cent*
Carcinoma	84	58
Mesothelioma	3	2
Adenoma	1	—
Organizing pneumonia	11	8
Lipoid pneumonia	4	3
Inflammation	14	10
Tuberculosis	6	4
Other lesions	20	15
TOTAL	143	100

False positives, 2; false negatives, 1.

diagnosed in 84 (58 per cent) instances, organizing pneumonia in 11 (8 per cent), and lipoid pneumonia in 4 (3 per cent). We made 2 false positive and 1 false negative diagnoses. In practically all cases of organizing pneumonia a clinical and radiographic diagnosis of cancer was made and the surgeon with his hand on the lung thought the lesion was cancer (Ackerman, Elliot, and Alanis, 1954). Frozen section diagnosis of organizing pneumonia is difficult because of the great cellularity, and in 1 instance an error was made because of this, but only a lobectomy was done.

The following case represents one of our false positive diagnoses:—

Case 13.—A 57-year-old white male was admitted to Barnes Hospital because of coughing and chest pain of 10 days' duration. Radiographic studies of the chest showed a left hilar mass and there was dullness to percussion on the left upper chest. The clinical and radiographic diagnosis was carcinoma of the lung. The

patient was explored and the left upper lobe was found to be extremely firm in consistency. A segment of the lower lobe was also indurated. A biopsy was obtained and the frozen section diagnosis was 'undifferentiated carcinoma' (*Fig.* 377). A left upper lobectomy and a segmental resection of the involved lower lobe was performed. The upper lobe weighed 410 g. and the pleura was thickened and presented many fibrous adhesions. The lobe was very firm in consistency and the cut surface was greyish-brown with many scattered small abscesses. This process involved the entire lobe. No evidence of tumour was found in the bronchi or lymph-nodes. Microscopical examination of the permanent paraffin sections revealed an inflammatory process in which the parenchyma of the lung was replaced by dense interwoven strands of cellular connective-tissue filling the alveoli. There was also a chronic inflammatory reaction, many giant cells, and multiple small abscesses.

Comment.—This was a very difficult diagnosis, but the possibility of an inflammatory process certainly has to be kept in mind. Fortunately a lobectomy in this particular case was indicated and it was adequate treatment. Cellular inflammatory cells growing between connective-tissue bundles may be mistaken for undifferentiated carcinoma. Secondary infection and pneumonitis are frequent in carcinoma of the lung secondary to obstruction of the bronchus or bronchioles by the tumour, so that a negative frozen section in an inflammatory lesion of this nature does not rule out the presence of carcinoma. Thorough inspection of the bronchus in these cases is extremely important for the inflammatory process may be secondary to a tumour. Round lesions thought to be tuberculoma radiographically, often are carcinoma. The peripheral bronchial adenoma, because of its cellularity, may be mistaken for undifferentiated carcinoma. However, if careful attention is given to the gross and this diagnosis is considered, the correct diagnosis can be made. The reaction to lipid in the lung may be difficult to evaluate because of the tissue reaction that it may induce. In typical well-delimited lipoid pneumonia the cut section may show fat on the surface and it may also have a greasy appearance. In diffuse lipoid pneumonia the radiographic and clinical pictures may exactly simulate cancer. There may even be apparent lymphangitic involvement of the pleural surface. But again, frozen section should be definitive. Also in a lesion of this type in which the entire lobe is involved, lobectomy is often indicated and, if done, careful examination of the bronchus to the lobe is imperative. Another problem is the undifferentiated cancer with large cells in which there is a great deal of inflammation. The inflammatory reaction may mask the presence of cancer.

PANCREAS

Frozen section of lesions of the pancreas and periampullary region is often considered extremely difficult. Practically all the references in the literature indicate that this is an unreliable method for the diagnosis of cancer (Maingot, 1955; Cattell and Warren, 1951). However, this has not been our experience (Spjut and Ramos, 1957). There are many possibilities of error, including aberrant ducts in the wall of the small intestine and pronounced chronic pancreatitis with atrophy and dilatation of acini which may be mistaken for carcinoma. It is often stated that incisional biopsy of the pancreas may result in implantation and spread of cancer over the peritoneal surface. We agree that there is such a risk, but this risk is far outweighed by the high mortality and pronounced morbidity of radical pancreatectomy. We had one definite implantation following frozen section diagnosis of carcinoma of the ampulla. Tumour later recurred in the skin of the abdomen. This was excised and the patient is free from disease 30 months after resection. Furthermore, although we do have cures in patients with carcinoma of the terminal one-third of the common bile-duct and ampullary region, we still have no cures for carcinoma of the head of the pancreas. At times in order to avoid the risk of implantation we have done needle biopsies and frozen section on the material obtained, which has proven in several occasions to be satisfactory.

Table XI.—Frozen Sections of Pancreas and Periampullary Region

Type of Lesion	*No.*	*Per Cent*
Carcinoma of the pancreas	39	57·3
Islet-cell adenoma	3	4·4
Carcinoma of the ampulla	6	8·8
Carcinoma of common bile-duct	1	1·4
Non-neoplastic lesions	19	27·7
Total	68	100

False positives, 0; false negatives, 6.

Case 14.—A 64-year-old widow entered Barnes Hospital on Nov. 18, 1954, complaining of 'bloating and belching' associated with intermittent left upper quadrant pain and anorexia. There was also a history of weight loss of 10 lb. in the month previous to admission. Four days prior to admission the stools became grey in colour and the patient developed icterus. The laboratory tests were consistent with obstructive jaundice. The patient was explored on Nov. 29 and a mass the size of a golf ball was discovered in the head of the pancreas. Frozen section of a lymph-node from the gastro-hepatic ligament was negative for cancer. A biopsy of the head of the pancreas showed chronic inflammation. The duodenum was opened and the ampulla found to be normal. A Vim-Silverman needle was introduced from the duodenum into the pancreas and frozen section of this material revealed carcinoma (*Fig.* 378) (Thorpe and Elman, 1955). A modified Whipple procedure was carried out. Permanent sections revealed carcinoma with nerve-sheath invasion and six lymph-nodes were negative for cancer.

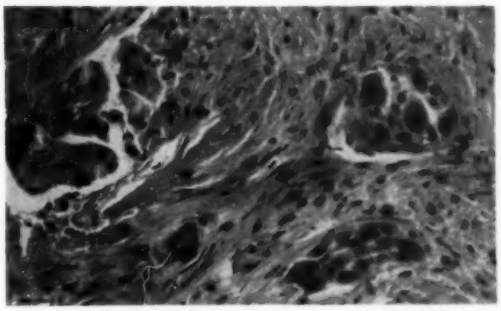

Fig. 378.—*Case* 14. Permanent section of a frozen section of a needle biopsy of the pancreas. Note nests of cancer cells growing in fibrous stroma. W.U. Ill. No. 57-7207. (× 185.)

Comment: In our series we diagnosed carcinoma in material obtained through needle biopsy in 3 instances. We have had no technical difficulties in doing frozen sections on these small pieces of tissue. At times this may be the only method by which the diagnosis can be established. It is true that if we see nerve-sheath invasion or obvious undifferentiated

carcinoma, or tumour within a lymph-node, the diagnosis is not difficult at all. However, our greatest difficulty is in those cases where the lesion arises from duct epithelium where the pattern of the tumour is difficult to differentiate from normal duct epithelium. In our series we did frozen sections on 68 lesions of the pancreas and periampullary region. Forty-nine were tumours and 19 were non-neoplastic in nature

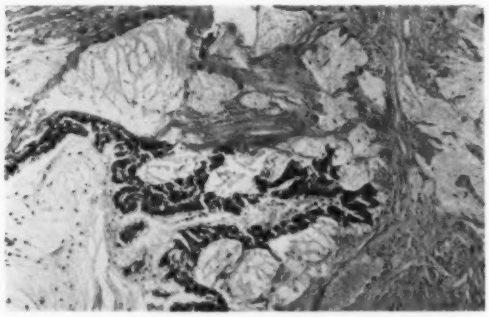

FIG. 379.—Photomicrograph of well-differentiated adenocarcinoma of the pancreas with excessive mucin production. Lesion was missed on frozen section because of the excessive mucin production. W.U. Ill. No. 56-6410. (× 65.)

(*Table XI*). The non-neoplastic conditions included chronic inflammation, pseudocysts, abscesses, and a benign proliferative lesion of the ampullary epithelium. Of 49 neoplasms, 42 were carcinomas and islet-cell adenomas of the pancreas, 6 were carcinomas of the ampulla, and there was 1 carcinoma of the common bile-duct. We had an accuracy of 91 per cent (6 errors in 68 cases). All 6 errors were made in the cancer group and in each instance it was a false negative diagnosis.

The errors included carcinoma that was missed because of excessive mucin production (*Fig.* 379), and 3 errors were made because of excessive fibrosis associated with only minimal carcinoma.

STOMACH

We have already discussed the risk of implantation in doing biopsies of the stomach and we have now reduced the number of frozen sections that we do in this organ. In this group of 58 cases we had no false positive diagnoses (*Table XII*) and we made 1 false negative diagnosis. This case follows:—

Table XII.—FROZEN SECTIONS OF STOMACH

Type of Lesion	*No.*	*Per Cent*
Carcinoma	16	27·6
Miscellaneous neoplasms	8	13·8
Chronic ulcer and chronic inflammation	30	51·7
Other lesions	4	6·8
TOTAL	58	100

False positives, 0; false negatives, 1.

Case 15.—A 55-year-old white woman entered Barnes Hospital because of a 2½ months' history of epigastric pain radiating to the left upper quadrant and not relieved by food. Gastroscopic examination revealed an annular lesion in the pars media with ulceration, and this was thought to be carcinoma. Radiographically the lesion was also thought to be carcinoma of the stomach. At operation there was a large lesion involving the pylorus and the regional lymph-nodes were enlarged. There were scattered small nodules throughout the liver which were thought to be metastases. The liver and a regional lymph-node were biopsied and no tumour was found on frozen section. The stomach was opened, therefore, and a biopsy of the suspicious area was taken and submitted for frozen section. Frozen section diagnosis was 'chronic inflammation'. A subtotal gastrectomy was done. Examination of the gross specimen showed two ulcers, one in the anterior and the other in the posterior wall of the stomach. The largest ulcer was 3 cm. in diameter. The permanent sections revealed carcinoma of the stomach, linitis plastica type. The permanent section of the material used for frozen section contained clusters of tumour cells growing between muscle-bundles intermingled with the inflammatory cells (*Fig.* 380).

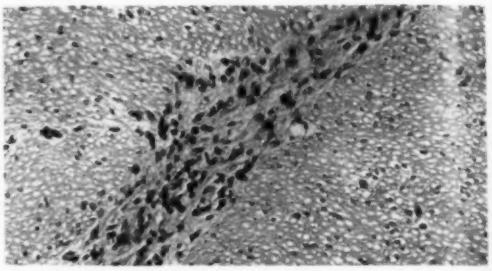

FIG. 380.—*Case* 15. Photomicrograph showing nests of cancer cells intermingled with chronic inflammatory cells growing between muscle-bundles of the stomach. Cancer cells can be recognized by their nuclear abnormalities. W.U. Ill. No. 57-4808. (× 160.)

Comment.—This type of lesion is extremely difficult to recognize on frozen section because the changes in the mucosa may be minimal and tumour cells will be found growing between muscle-bundles. They will have no gland pattern and will also be associated with chronic inflammatory cells and their recognition will depend on their nuclear abnormalities.

We do not as a rule do frozen sections on ulcers of the stomach unless they are high in the lesser curvature. On occasions we do frozen sections on polypoid lesions and frequently such lesions turn out to be epithelial in nature and in other instances they turn out to be smooth-muscle tumours, heterotopic pancreas, or even a lipoma. The exact diagnosis in such lesions may considerably modify surgery. We have seen a fair number of instances in which a patient with gastric symptoms had a constant defect demonstrated radiographically in the stomach interpreted as possible cancer. At the time of operation the surgeon feels no abnormality and on opening the stomach sees no abnormality. Under these circumstances we think it is important that the surgeon makes a biopsy of the area and requests a frozen section, otherwise he may miss superficial spreading cancer; but, most important, if the frozen section turns out to be negative this can be reassuring to the patient and helpful to the radiologist. From the practical standpoint, in these instances where the surgeon felt and saw no abnormality with the stomach open even if the radiologist saw an abnormality, in all instances in our experience there was no evidence of cancer. In a few instances the diagnosis of lymphoma has been made. This diagnosis

is important in determining treatment, or abandoning surgery in favour of irradiation therapy. The diagnosis of the extension of cancer to the peritoneum or distant lymph-nodes frequently modifies the extent of the surgery. The following case is representative:—

Case 16.—A 56-year-old white male entered Barnes Hospital because of gastric symptoms. A diagnosis of carcinoma of the stomach was made radiographically. Clinically the patient was also thought to have carcinoma.

FIG. 381.—*Case* 16. Photomicrograph of mucosa of the stomach showing evidence of gastritis with intestinalization of the glands. W.U. Ill. No. 57-4807. (× 67·5.)

Gastroscopic examination also revealed a suspicious area in the stomach with loss of the mucosal pattern. At operation no abnormality was felt and a gastrostomy was done and the suspicious area biopsied. Frozen section diagnosis was 'chronic gastritis' (*Fig.* 381), therefore, nothing further was indicated. If no frozen section had been done, a subtotal gastrectomy would have been done unnecessarily. We feel that frozen sections should be done in these cases.

At times a benign chronic perforating ulcer may be associated with a large, pergastric inflammatory mass. This mass is often fixed to the liver or the head of the pancreas. In such instances if the lesion is cancer the possibilities of cure are small. However, if definitive surgery is done, this may imply partial resection of the liver, pancreas, and spleen. But if the lesion is benign, conservative partial resection is done, leaving the bed of the ulcer in place. In a group of huge gastric ulcers frozen section was done under these circumstances in 6 cases and the mass and the edge of the ulcer were biopsied and conservative surgery was done (Shoulders and Lischer, 1953). Another indication for frozen section is if a patient has a large tumour of the stomach in which total removal would mean total gastrectomy. Bricker (1956) advocates a frozen section under these circumstances, for if the lesion is a lymphosarcoma he would refer such a patient for irradiation therapy.

SKIN AND ORAL CAVITY

As can be seen from our *Table I*, we did 35 frozen sections on skin and 22 on the oral cavity. It is our feeling that practically all of these were not clinically indicated. The lesions of the skin and oral cavity are easily accessible to incisional biopsy and with permanent sections therapy can be carefully planned. In skin cancer we have employed frozen section to determine the adequacy of a surgical excision.

MISCELLANEOUS

The last 65 frozen sections comprise an extremely heterogeneous group. In frozen sections of the gall-bladder the question is usually to determine the presence or absence of cancer. In the œsophagus peptic ulceration may sometimes resemble carcinoma. We have seen benign lesions of the œsophagus such as leiomyomas and heterotopic gastric mucosa. In the gynæcology group we do few frozen sections. We see little or no indication to do frozen sections of the cervix. There is no difficulty in doing such frozen sections or even interpreting endometrial curettings. However, we cannot freeze all the endometrial curettings, and it is best to wait for their thorough processing in order to plan adequate therapy. The proof of extension of carcinoma of the cervix to regional lymph-nodes often either modifies an operative procedure or causes the surgeon to abandon the operation. The proof of endometriosis is usually of a confirmatory nature. The microscopical proof of the exact type of ovarian tumour may determine how extensive the operative procedure should be—in other words, whether the opposite ovary and the uterus should be removed. The other frozen sections done on other organs make such a heterogeneous group that no further comment is justified. Frozen sections for the otolaryngologist and neurosurgeon have not been included in this review, but our record in these fields is comparable to those cited.

CONCLUSIONS

1. Frozen section diagnosis is a highly accurate method of diagnosis. There were 1269 frozen sections, 4 false positives and 22 false negatives, with an over-all accuracy of 98 per cent. This method achieves its highest accuracy when there is co-operation between an experienced surgeon with an interest in pathology, and a pathologist with a clinical viewpoint.

2. The primary reason for doing a frozen section is *to make a therapeutic decision* at the time of operation. There are certain limitations to this method and these limitations vary with the organ and the clinical conditions encountered.

3. The risk of cancer implantation during frozen section has been emphasized, particularly in lesions of the thyroid, lung, stomach, and pancreas.

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CARDIOVASCULAR CHANGES IN THE POST-GASTRECTOMY SYNDROME

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IT is well recognized that gastrectomy and gastro-enterostomy produce post-prandial symptoms in some patients (Hertz, 1913; Ryle, 1934; Zollinger and Hoerr, 1947; Gilbert and Dunlop, 1947; Irvine, 1948; Adlersberg and Hammerschlag, 1949; Muir, 1949; and Smith, 1951). It has also long been known that attacks of hypoglycæmia follow meals in some of these patients (Christlieb, 1938; Evanson, 1942), and this was considered the most likely cause of these upsets by some authors (Gilbert and Dunlop, 1947).

Adlersberg and Hammerschlag (1949) were the first to clarify the situation, dividing their patients into two groups, depending on whether the symptoms appeared early or late after the meal. The early symptoms, epigastric pressure, nausea and fullness, eructation and belching, dizziness, and occasionally bilious vomiting occurred immediately after the meal and were associated with hyperglycæmia. The late symptoms, occurring 2½–3 hours after the meal, were characterized by fatigue, weakness, and perspiration, and were associated with hypoglycæmia. The great majority of patients fall into Adlersberg and Hammerschlag's early group and the late hypoglycæmic attacks are a rare cause of disability (Irvine, 1948; Muir, 1949).

The cause of this early group of symptoms remains obscure. It has already been noted that the blood-sugar is often raised during the symptoms, and this hyperglycæmia has been considered the causal factor by Glaessner (1940). Mechanical distension of the jejunum by rapid emptying through the gastric stoma has been thought important (Custer, Butt, and Waugh, 1946), and Smith (1951) appeared to show that precipitate gastric emptying was a feature of dumpers but not of non-dumpers. Machella (1949) has claimed to reproduce the symptoms by mechanically distending the upper jejunum with a balloon. Roberts, Randall, Farr, Kidwell, McNeer, and Pack (1954), on the other hand, could only produce a sense of fullness in the epigastrium by such mechanical stimulation. Sympathetic stimulation has been considered a factor in the production of these early symptoms (Irvine, 1948; Smith, 1951; Roberts and others, 1954). Certainly the flushing, sweating, tachycardia, and dizziness are compatible with adrenaline release, and some authors (Smith, Fraser, Staynes, and Willcox, 1953) have reproduced those symptoms in their patients by adrenaline administration. Eosinopenia also has been noticed during these attacks of dumping (Pontes and Neves, 1953), and Pulvertaft (1954) was able to demonstrate a rise in the blood catechol amines, but this did not correlate with symptoms nor was the rise greater than that obtained under similar conditions in normal people.

The muscular weakness which is a part of the syndrome has been ascribed to a lowering of the serum-potassium (Smith, 1951; Smith and others, 1953) which was observed during dumping attacks and was associated with E.C.G. changes characteristic of hypokalæmia. This hypokalæmia could be explained by the rapid glycogen formation following on the fast glucose absorption, a process known to fix potassium in the liver cells (Harrop and Benedict, 1922; Fenn, 1939). Intravenous infusion of potassium prevented the muscular weakness of the syndrome and reversed the E.C.G. changes. Rochlin and Edwards (1954) have observed similar E.C.G. changes following the ingestion of 100 g. of glucose in normal subjects with intact stomachs, these changes being prevented by the addition of 3 g. potassium chloride to the meal. However, Goldberger (1954) states that potassium has a general tendency to reverse the direction of abnormal T waves regardless of the cause of the abnormality. In addition Smith (1951) considered that the release of an adrenaline-like substance might account for some of the symptoms and this might be expected to increase the K depletion (Castleden, 1937). Roberts and others (1954) failed to correlate the symptoms with low levels of serum-potassium. They also observed low plasma-potassium levels after glucose administration. However, in the experiments showing a drop in plasma-potassium they noted that the sequence was such that cardiovascular alterations and symptoms occurred prior to the hypokalæmia. In addition, a fall in plasma-potassium was recorded in patients with intact stomachs after a glucose meal with no cardiovascular upset and no symptoms.

Yet another factor which has been considered of importance in producing these symptoms has been changes in blood-volume (Roberts and others, 1954; Roberts, Randall, Bain, Medwid, and Schwartz, 1955; Walker, Roberts, Medwid, and Randall, 1955).

Roberts and others (1954) measured blood-volume and serum-potassium, and obtained E.C.G. recordings in a group of gastrectomized patients before and after administration of hypertonic solutions of glucose by mouth. Following ingestion of the glucose solution typical dumping symptoms appeared in 10–15 min., and these were associated with a marked decrease in the blood-volume which was noticed within 10 min. and maximal in 30–40 min. During the same period E.C.G. changes similar to those described by Smith (1951) appeared. The authors concluded that the potassium changes were secondary to the deposition of glycogen and not the major cause of either the E.C.G. changes or the symptoms. In most of these patients the decrease in plasma-volume was associated with hypotension which they thought might result in sympathetic stimulation from presso-receptors in the aortic arch, and their E.C.G. findings were explained on the basis of coronary insufficiency from reduced blood-flow or sympathetic stimulation. Amdrup and Jørgensen (1956, 1957) also observed changes in plasma-volume after ingestion of hypertonic glucose solution in patients after gastrectomy. The plasma-volume fell in those patients with dumping symptoms, while it rose in those not affected. E.C.G. tracings and blood-pressure and pulse changes were not reported.

Hinshaw, Jørgensen, Davis, and Stafford (1957), in a similar study, noted that some of their patients had decreases in plasma-volume without actual dumping symptoms, and these observations suggested to them that some other factors might play a significant part in the aetiology of the syndrome. Digital plethysmography studies demonstrated a rise in peripheral blood-flow concomitant with the plasma-volume decrease in patients with marked symptoms. They suggested that an increase in peripheral blood-flow of several times the control values would involve a peripheral intravascular shift of considerable quantities of blood and could result in reduced blood-flow to central vital areas such as the brain and heart. They thought that the increased peripheral flow was more important than the plasma-volume shift, since patients with minimal symptoms had no increased peripheral flow and yet often had marked shifts in plasma-volume. Conversely, severe dumping symptoms were always associated with a considerable rise in peripheral blood-flow. Zollinger (1957) has also noticed plasma-volume shifts occurring in patients after partial gastrectomy who had no post-prandial symptoms.

The present study was undertaken to examine further the cardiovascular changes which follow the ingestion of hypertonic glucose in patients after partial gastrectomy and gastro-enterostomy. Pre-operative studies of identical nature were also done in these patients in the hope that an abnormal response could be detected in those who later developed severe post-gastrectomy symptoms. In addition, since a gastrectomy with gastroduodenal anastomosis (Billroth I) has been said to be associated with less severe post-prandial upset than operations with gastrojejunal anastomosis (Polya) (Capper and Butler, 1951; Harkins, Schmidt, Nyhus, Kanar, Zech, and Griffith (1954), patients with dumpings after gastrectomies were studied in a similar manner before and after conversion to a gastroduodenal anastomosis.

MATERIAL AND METHODS

Thirty-six experiments are reported on 27 patients who were studied in the following groups:—

a. Patients with intact stomach before operation for peptic ulcer, 10 studies.

b. Patients after Polya gastrectomy, 17 studies.

c. Patients before and after conversion from Polya to Billroth I gastrectomy, 4 studies.

d. Patients after gastro-jejunostomy, 5 studies.

The results will be reported under these groupings. Patients were studied in the sitting position after a 12-hr. fast. For 1 hr. before and 1 hr. after the oral intake of 100 ml. 50 per cent glucose, pulse-rate, blood-pressure, and E.C.G. recordings were done at frequent intervals and hæmoglobin, packed-cell volume, blood-sugar, and serum-potassium estimations were done every 15 min.

Table I.—Deviation from Constant Disappearance Rate of Radioactive Human Serum Albumin (I^{131} HSA) in 12 Normal Patients

Time after Injection of I^{131} HSA (min.)	*Standard Deviation Percentage from Constant Disappearance Rate*
15	±2·7
30	±1·7
45	±1·3
60	±1·8
75	±0·7
90	∓0·9
105	±1·6

Plasma-volume estimations were made by determining a change in the disappearance rate from the peripheral blood of human serum albumin tagged with radio-active iodine (I^{131} Human Serum Albumin), a dose of 15 μc. being used. Pritchard, Moir, and MacIntyre (1955) have shown, using whole blood, that the disappearance rate of I^{131} human serum albumin is constant in the first 2 hr. after I.V. injection. Twelve normal patients were studied to find whether the same would apply with intermittent sampling of plasma. The range of variation from a constant disappearance rate is shown in *Table I* and readings more than twice the standard deviation were taken as significant. From this table it will be seen the standard deviation is least between 1 and 1½ hr. after the injection of I^{131} human serum albumin and the meal was, therefore, given 1 hr. after the injection.

The use of a disappearance curve to measure the change in plasma-volume produced by this test was checked further by making intermittent determinations of plasma-volume in some of these patients using repeated injections of Evans Blue as described by Plentl and Gelfand (1954). The Evans Blue concentration of plasma samples was estimated by absorption on to cellulose followed by elution with acetone (Bedwell, Patterson, and Swale, 1955). Similar results were obtained. Changes in plasma-volume are expressed as a percentage of the control level.

Blood-sugar estimations were done by the method of Hagedorn and Jensen (1923) and serum-potassium by flame photometry. A Cambridge Electrite machine was used for electrocardiographic tracings. The standard three leads and the augmented V leads were used. The electrodes were not moved during

the period of study. Only patients with normal electrocardiographic tracings in the control period were accepted for this experiment, and all patients had an hæmoglobin of 12 gm. per cent or over.

3. Dumping. When epigastric fullness was associated with vasomotor symptoms this was recorded as dumping and the severity graded as moderate or severe.

Table II.—Cardiovascular Changes after a Glucose Meal in Patients after Partial Gastrectomy (Polya Type)

Patient	Rise in Pulse-rate (Min.)		Rise or Fall in Blood-pressure (Mm./Hg)		E.C.G. Changes	Percentage Reduction in Plasma-volume after Glucose (Min.)			Symptoms
	Before Glucose	After Glucose	Before Glucose	After Glucose		15	30	45	
1	84	122	110/80	120/80	No change	8	8	4	Severe
2	80	112	95/65	110/70	P peaked T_2, T_3, flat at 14 min. ST–T, sagging; T_3 inverted at 20 min.	11	13	10	Severe
3	70	88	120/90	70/?	P, peaked T_2, T_3, inverted by 20 min. ST–T, sagging; U-waves appear	10	12	12	Severe
4	60	110	110/80	70/?	P, peaked T_2, flat; T_3, inverted at 23 min. ST–T, sagging	25	13	0	Severe
5	72	92	135/90	145/95	P, no change T_2, T_3, flat; T_3, inverted at 23 min. ST–T, sagging and U-waves 9–40 min.	4	12	22	Severe
6	80	106	100/70	85/55	No change	Nil	20	—	Severe
7	84	102	110/80	90/60	No change	—	16	—	Severe
8	70	100	No change		Not done	11	6	—	Moderate
9	68	100	135/100	160/100	P, peaked T_2, T_3, aVF, flat, 18–30 min. ST–T, sagging in Lead 2 and aVF	5	10	7	Moderate
10	No change		No change		P, no change T, aVF, flat at 18 min., normal at 32 min. U-wave, aVF 18 min.	2	3	—	Moderate
11	64	96	No change		P, peaked T_2, T_3, T, aVF flat, 10–20 min., restored at 35 min. U-wave, 2 aVF	8	14	4	Moderate
12	No change		No change		P, peaked T_2, T_3, T, aVF flattened, 15–20 min.	2	4	—	Moderate
13	78	120	110/70	130/70	Not done	19	16	8	Epigastric fullness
14	86	120	105/70	120/75	P, slight peaking T_2, T_3, flat, then inverted, 15–48 min. ST–T, sagging, 15–48 min.	14	6	6	Epigastric fullness, slight nausea
15	80	98	No change		P, no change T_2, T, aVF flattening	2	—	4	Epigastric fullness, slight nausea
16	50	60	No change		No change	8	9	8	Nil
17	78	90	No change		P, no change T_2, slight flattening (maximum at 27 min.)	5	6	4	Nil

Recording of Symptoms.—An effort was made to record precisely at what time the symptoms occurred. This frequently compelled the observer to ask direct questions about various symptoms, since the patients were often slow to state the time of their onset or change in character.

The severity of symptoms was assessed as follows:—

1. No symptoms.

2. Epigastric fullness (by itself this was not assessed as dumping).

RESULTS

Pre-operative studies are reported first. Next, the cardiovascular response noted in each of the post-operative groups will be described and the presence or absence of E.C.G. changes noted.

Cardiovascular Response of Patients with Intact Stomach to Ingestion of 100 ml. 50 per cent Glucose.—In most of these patients the glucose meal was followed by a rise in pulse-rate. The blood-pressure either showed no change or rose slightly.

Plasma-volumes tended to decrease slightly (2–4 per cent) in the first 30 min. after the meal. Electrocardiographic changes, of a type similar to those noted later, were seen in 1 patient. Epigastric fullness without vasomotor changes was noted in 1 patient.

Cardiovascular Response to Glucose Meal in Post-operative Patients.—

1. *After Polya Gastrectomy.*—The changes in pulse, blood-pressure, plasma-volume, and E.C.G. hypotension during the attack, but they had severe symptoms. In the remainder the blood-pressure was either maintained or elevated.

2. *Before and After Conversion from Polya to Billroth.*—The cardiovascular changes after a glucose meal in 4 patients with Polya gastrectomy are compared with identical studies in the same patients after a change to a gastroduodenal anastomosis. The results obtained are set out in *Table III*. It will be noticed that the responses were of similar magnitude

Table III.—Cardiovascular Response to Glucose Meal before and after Conversion from Polya to Billroth I Gastrectomy in Gastrectomized Patients

Patient	Pulse-rate (Min.)		Blood-pressure (Mm./Hg)		Maximal Reduction in Plasma-volume	Symptoms
	Before Glucose	After Glucose	Before Glucose	After Glucose		
A: Polya	84	112	100/80	120/80	Per cent 8	Severe
Billroth I	88	126	115/85	140/90	5	Moderate
B: Polya	80	112	95/65	110/70	13	Severe
Billroth I	68	148	90/60	110/70	20	Severe
C: Polya	80	106	100/70	85/55	20	Severe
Billroth I	76	90	95/70	85/60	15	Moderate
D: Polya	86	120	105/70	120/75	14	Moderate
Billroth I	92	130	95/70	145/90	12	Moderate

are shown in *Table II*, with the degree of upset noted. In all patients a significant reduction in plasma-volume was noted in the first 30 min., ranging from 10–16 per cent in most patients. Packed-cell volumes rose in proportion. But shifts as high as 25 per cent after the second operation, and the symptoms were of equal severity in 2 cases.

The test-meal used in these studies was 100 ml. 50 per cent glucose, and it may be that this was too severe a test to discern any improvement in these

Table IV.—Cardiovascular Changes after Glucose Meal in Patients after Gastro-enterostomy

Patient	Rise in Pulse-rate (Min.)		Rise or Fall in Blood-pressure (Mm./Hg)		E.C.G. Changes	Percentage Reduction in Plasma-volume after Glucose (Min.)			Symptoms
	Before Glucose	After Glucose	Before Glucose	After Glucose		15	30	45	
1	64	72	No change		No change	5	19	6	Moderate
2	68	80	100/80	70/?	No change	7	—	—	Moderate
3	58	80	No change		P, no change T_2, T_3, aVF slight flattening; T_3 inverted	7	6	—	Nil
4	64	80	95/65	105/75	No change	5	3	—	Nil
5	65	84	No change		Left heart strain (excluded)	11	9	5	Nil

and as low as 2 per cent were found. It was noted that the extent of the fall in plasma-volume showed no correlation with the degree of upset. Marked symptoms could occur with a small shift, and a large diminution could occur with no symptoms or only epigastric fullness.

In all but 2 of the patients the fall in plasma-volume was associated with a marked tachycardia. Only 4 of the 12 patients who 'dumped' had patients. Two of the 4 patients were cured of bilious vomiting after food, and perhaps a further patient could be considered to have less disability from dumping after normal meals.

3. *After Gastro-enterostomy.*—The responses of 5 patients after gastro-enterostomy are recorded in *Table IV*. These results were similar to those noted in the gastrectomy patients, but less marked, and dumping symptoms occurred in 2 patients.

The E.C.G. Studies.—The cardiographic changes noted during the tests are recorded in *Tables II* and *IV*. Most had reverted completely to normal within an hour of the glucose meal, but some still showed minor alterations. The changes tended to fall within a similar pattern:—

1. Lowering and flattening of the T wave.
2. Sagging of the S–T interval.
3. In 7 cases peaking of the P wave.

Varying degrees were present and are fully analysed below:—

	Electrocardiograms	
Patients	*No Change*	*Pattern Present*
Pre-operative (10)	9	1
After gastrectomy (15)	4	11
After gastro-enterostomy (5)	4	1

Rhythm: Sinus rhythm was unchanged in all cases except one, in which a Wenckeback phenomenon was observed.

Heart-rate: The heart-rate was increased in all cases, apart from six in which no change was noted.

P *Wave*: In seven of the post-gastrectomy cases increased voltage with peaking of the P wave was noted during the period of cardiographic changes, 10–20 min. after the glucose drink. This change in the P wave was consistently most marked in Leads II, III, and aVF; returning to normal voltage by the end of each test.

Q–T ratio: This was calculated by the method of Goldberger (1954) and was noted to increase in all but six cases.

QRS: In a few cases with right axis deviation, if T wave changes were noted, there was an increase in the voltage of S in Lead I. Otherwise, no change in the electrical axis of the heart occurred.

ST *Segment and* T *Wave*: The T wave tends to broaden and flatten; it may become inverted, especially in Lead III. With these changes there is a sagging of the S–T segment and in some cases a low take-off below the iso-electric line. These changes are quite characteristic and are only noted in Leads II, III and aVF, occurring 10–20 min. after the glucose and with no corresponding S–T elevation in Leads I, aVL, or aVR.

U *Wave*: In some cases the U wave was accentuated and became easily seen, but then it was difficult to separate from the T wave, the two tending to run together.

As can be seen from *Tables II* and *IV*, E.C.G. changes were not invariably associated with symptoms nor in any way related to plasma-volume alteration.

Effect of Sympathetic Blocking Drugs on E.C.G. Changes.—Repeat studies were done on 5 patients who showed obvious changes after the glucose meal. They were given 0·5 mg. ergotamine tartrate intravenously once the changes were established. The duration of alteration in E.C.G. tracing was considerably shortened in all cases as compared with the initial studies.

Blood-glucose.—The blood-sugar rose after the glucose meal and symptoms when present occurred during the period of hyperglycæmia. Neither the severity of the symptoms (*Fig.* 382) nor the reduction in plasma-volume showed any correlation with the blood-sugar level or the rapidity of its rise.

The rise in blood-sugar was most rapid in those patients with gastrojejunal anastomosis. In the 4 patients converted from a gastrojejunal to a gastroduodenal anastomosis a marked lessening in the rate of glucose absorption did not alter their symptoms or plasma-volume shift. Further confirmation that the rate of glucose absorption was independent of the symptoms was obtained in 3 patients who were given

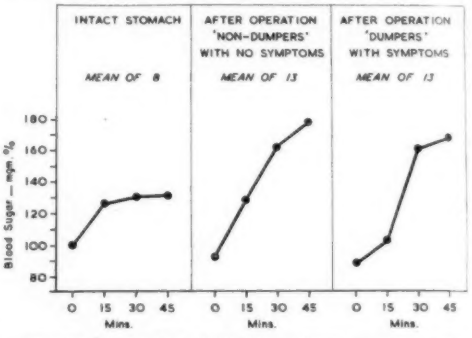

FIG. 382.—Comparison of blood-sugar levels in patients with and without symptoms.

100 ml. of 50 per cent fructose. Equivalent plasma-volume shifts and symptoms were noted, but a much less rapid rise in blood-sugar took place.

Serum-potassium.—Serum-potassium estimations were done in 12 patients with dumping symptoms and no constant trend was found. The range of readings was within normal, being 14·5–20·5 mg. per cent, but in 6 patients the serum-potassium fell as the test progressed, the final estimation still being within the normal range 1½ hr. after the glucose meal.

DISCUSSION

It would appear from these studies that after partial gastrectomy the ingestion of 100 ml. 50 per cent glucose is followed in all cases by a tachycardia and a significant fall in the plasma-volume, but there was no correlation between the size of this fall and the severity of symptoms, and patients with no symptoms also had equivalent reductions in plasma-volume. This agrees with the findings of Hinshaw and others (1957) and Zollinger (1957). In the light of these results it is hard to see any direct relationship between the reduction in plasma-volume and the production of symptoms, nor is it easy to explain the symptoms on the basis of the shift in plasma-volume causing hypotension, when in most cases the blood-pressure did not fall. This does not confirm the opinion of Roberts and others (1954). Some authors (Roberts and others, 1954; Amdrup and Jørgensen, 1956) believe this shift in plasma-volume is due to the passage of fluid into the intestinal lumen. Nor has the rate of glucose absorption into the blood-stream shown any direct or inverse correlation with symptoms or the degree of shift in fluid volume.

In addition, the fructose experiment and the studies after conversion to gastroduodenal anastomosis argue against the rate of glucose absorption being an important factor.

The serum-potassium results produced no evidence of hypokalæmia during the period of symptoms. It is well known that a normal serum-potassium level does not exclude an intracellular deficiency in potassium (Goldberger, 1954) and most commonly associated with potassium deficiency. However, all these changes can be produced by sympathetic stimulation (Hartwell, Burrett, Graybiel, and White, 1942) with, in addition, an increase in the voltage of the P wave. A study of *Table II* shows that

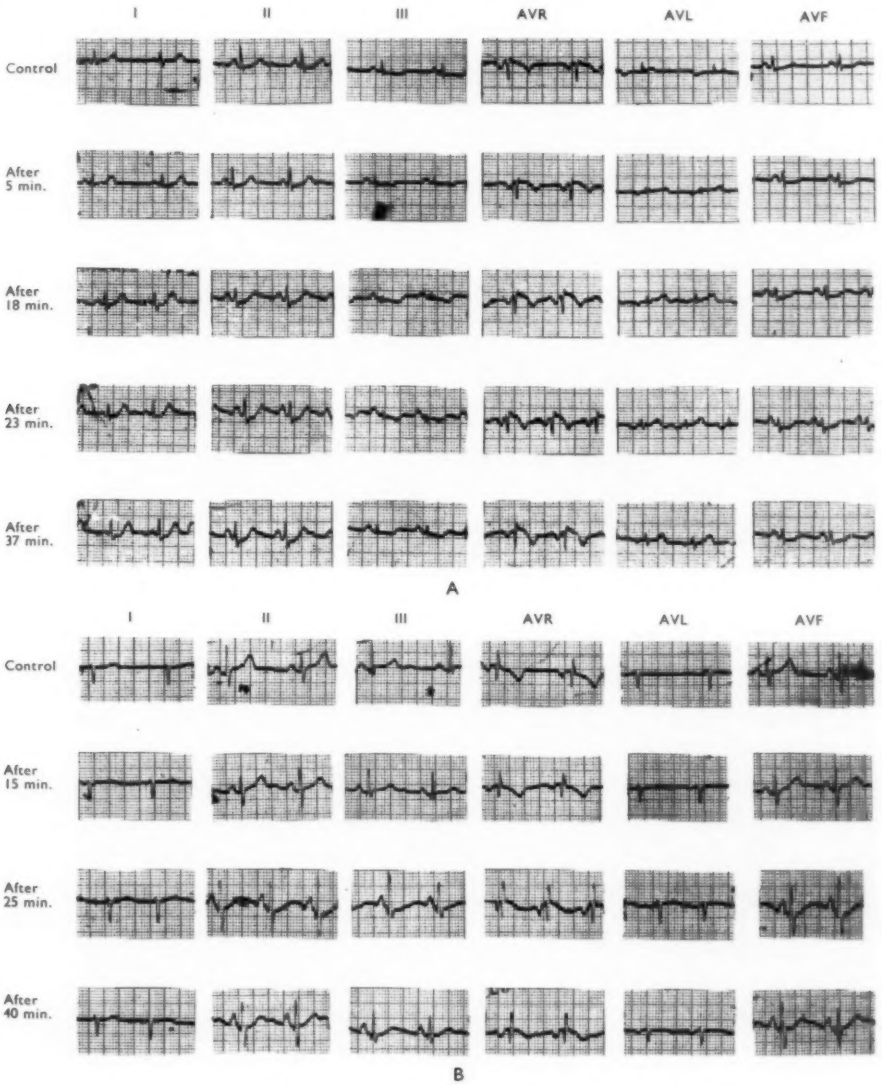

FIG. 383.—A, B, Electrocardiographic changes following a glucose meal after gastrectomy.

certainly E.C.G. changes occurred in many patients during the symptoms which are not dissimilar to those seen in potassium depletion (Bellet, Steiger, Nadler, and Gazes, 1950). The sagging of the S–T segment, flattening and inversion of the T wave, prolongation of the QT ratio, and the appearance of U wave which occurred in these patients, are those 7 of the patients having symptoms had significant peaking of the P wave. Furthermore, all the changes seen in these studies were confined to Leads II, III, and aVF, and this is claimed to be a feature of sympathetic stimulation (Nordenfeldt, 1941; Goldberger, 1954). Neither the character of the cardiographic patterns nor their unvarying distribution

lends any support to the suggestion that acute myocardial anoxia is their cause (Roberts and others, 1954).

A further pointer which perhaps supports sympathetic stimulation as a possible cause of the E.C.G. changes is the ability of ergotamine tartrate, a sympathetic blocking drug, to abolish their presence within a few minutes of intravenous injection.

The cardiographic tracings of 2 patients, typical of those seen in this study, are shown in *Fig.* 383 and the effect of intravenous ergotamine tartrate is shown in *Fig.* 384.

In conclusion, no evidence has been found to support the view that the plasma-volume changes which occur following a meal in a patient with a partial gastrectomy are the cause of the dumping syndrome.

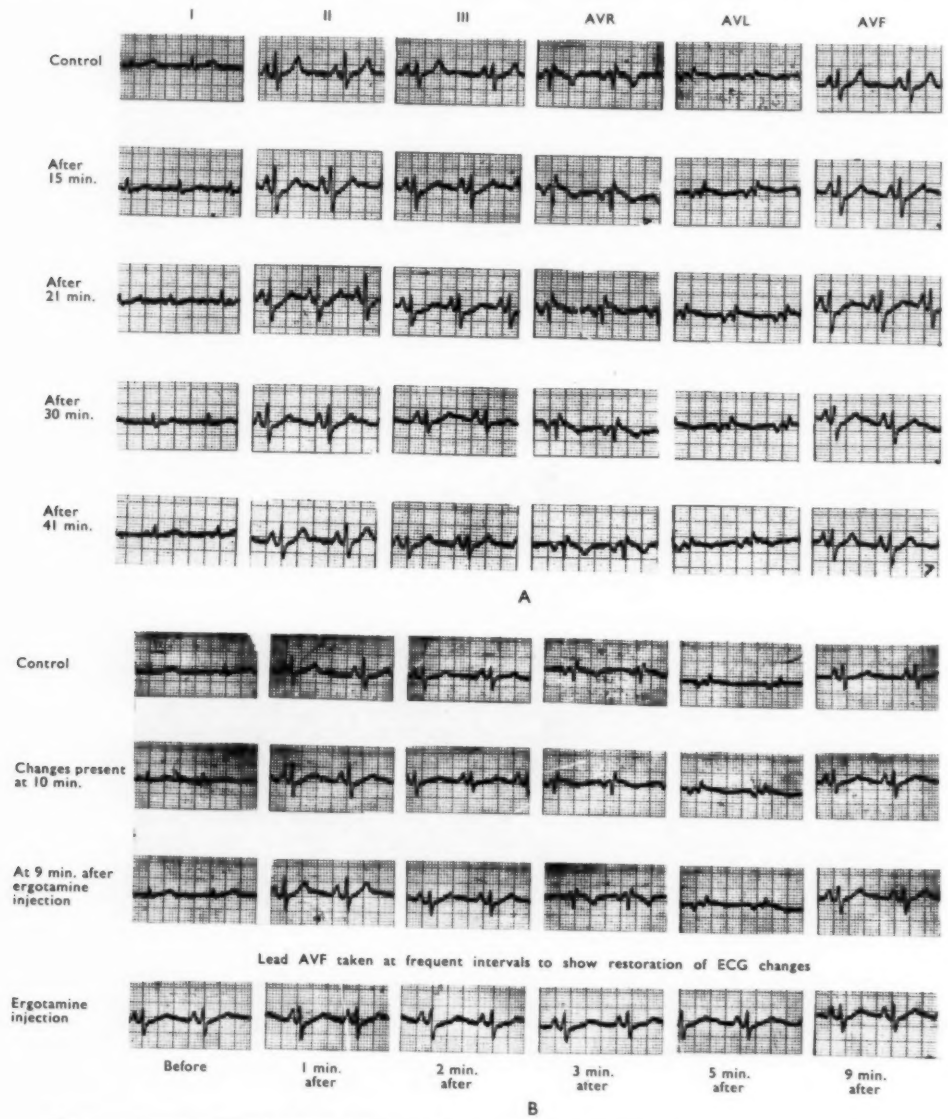

FIG. 384.—Electrocardiographic changes following a glucose meal after gastrectomy. A, Glucose meal alone; B, Glucose meal followed by intravenous ergotamine tartrate.

The serum-potassium was not lowered during the symptoms, and, though the E.C.G. tracings occurred during the syndrome which were not dissimilar from those seen in hypokalæmia, evidence has been produced suggesting that sympathetic stimulation may be their cause. The possibility that sympathetic stimulation accounts for other features of the syndrome bears further study.

The 4 patients who underwent conversion from gastrojejunal to gastroduodenal anastomosis showed no change in their cardiovascular response to a glucose meal, and, apart from bilious vomiting, the symptoms remained. This does not support the use of this procedure for the dumping syndrome unless bilious vomiting is the main feature.

The pre-operative glucose meals used in this study did not produce any cardiovascular response which would allow of correlation with dumping symptoms later. In view of the E.C.G. findings in this study, it would be of interest to relate the cardiographic response to posture before operation to the later incidence of dumping.

SUMMARY

1. The post-gastrectomy syndrome has been studied in a group of 27 patients before and after gastrectomy and gastro-enterostomy by noting pulse, blood-pressure, plasma-volume, blood-sugar, serum-potassium, and electrocardiogram following a glucose meal.

2. No abnormal cardiovascular response was noted in the pre-operative studies.

3. Reduction in plasma-volume occurred in all patients after gastrectomy and gastro-enterostomy, but no correlation was found between the size of shift and the presence or absence of symptoms.

4. Blood-sugar estimations following the glucose meal revealed no difference between 'dumpers' and 'non-dumpers'.

5. The serum-potassium was not low during the period of symptoms.

6. E.C.G. changes occurred in most patients during the symptoms. The alterations noted were more in keeping with sympathetic stimulation than with potassium depletion.

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CORROSIVE STRICTURE OF THE STOMACH

CASE REPORT AND REVIEW OF LITERATURE

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STENOSIS of the stomach due to corrosives, with sparing of the œsophagus, is sufficiently uncommon to merit reporting of the following case.

CASE REPORT

HISTORY.—D. H., a man aged 37 years, presented himself on March 2, 1957, complaining of frequent attacks of vomiting occurring two to three hours after meals. His previous history is as follows:—

He had been perfectly well until Feb. 6, 1957, and had suffered from no dyspepsia. He is emotionally unstable and his domestic life has been rather a disturbed one. These were the circumstances that led up to his consumption of 3 oz. of concentrated hydrochloric acid on a fasting stomach at 6 p.m. on the above date. He complained of a feeling of "burning in the stomach" at 6.40 p.m., and shortly after this effective emesis occurred with the aid of emetics. At 7 p.m. he was admitted to hospital, given egg and milk, and treated with gastric lavage. At the time he was vomiting blood. He recovered and was discharged and it was twenty-one days after the consumption of acid that he began to vomit after meals. Obviously a stenotic lesion had developed as he described his symptoms in the following rather graphic fashion—i.e., "jerks and stoppages and pain" in the epigastrium and "a rippling passing from left to right".

FIG. 385.—Barium-meal examination, showing prepyloric stricture, antral pouch, and normal-looking duodenal cap.

On March 14 barium-meal examination (*Fig.* 385) showed a normal œsophagus and gross narrowing of the distal part of the stomach in the prepyloric region. Beyond this, a small antral pouch and a normal-looking duodenal cap were seen to fill with barium. Emptying was slow and there was a large six-hour residue (*Fig.* 386).

His vomiting increased in volume and in frequency, and on March 27 he was admitted to hospital for exploratory laparotomy.

ON EXAMINATION.—There was no evidence of scarring in the mouth. He was thin and wasted and a stomach splash was present.

AT OPERATION (April 4).—He was found to have almost complete stenosis of the stomach in the prepyloric region, there being a small antral pouch between the stricture and the sphincter (*Fig.* 387) and thus a variety of hour-glass deformity. The stomach proximal to the constriction was considerably dilated. A Billroth I partial gastrectomy was performed, and he made an uneventful recovery.

FIG. 386.—Barium-meal examination, showing dilated stomach with large six-hour residue.

He was seen in a follow-up clinic on June 6 when he was found to be very well, having gained 2 st. in weight.

PATHOLOGY REPORT.—

Stomach.—Gross: A segment of stomach showing an annular constriction with visible puckering externally. There is a proximal orifice about 1 mm. diameter (*Fig.* 388) which leads into a tract 4 mm. long. The tract appears to be lined by mucosa.

Histology: The constricted portion of stomach shows very extensive fibrosis in the submucosa. In this region the muscularis mucosæ has been destroyed but the mucosa appears to have regenerated. The fibrous submucosa immediately adjacent to the stenosed lumen contains many blood-vessels which are surrounded by lymphocytes. The submucosal fibrous tissue obviously has contracted and drawn in the mucosa and external muscle coats of the stomach (*Fig.* 389). There is a little patchy fibrosis of the muscle wall indicating penetration of the original acute ulceration to this depth.

DISCUSSION

The ingestion of corrosive substances is of common occurrence and resulting stricture of the œsophagus is often described. Sometimes the stomach is involved at the same time. Corrosive stricture of the stomach with an undamaged œsophagus is an uncommon lesion. Strode and Dean (1950) reviewed 140 cases of pyloric stenosis with

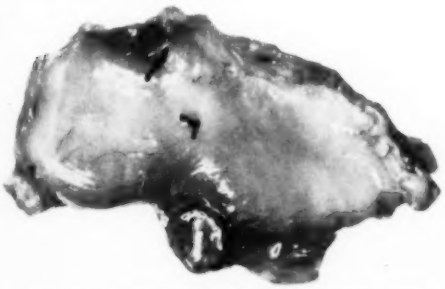

FIG. 387.—Segment of stomach, showing stricture marked by black sutures and small antral pouch. Note retained peritoneal sheen. (× ⅓.)

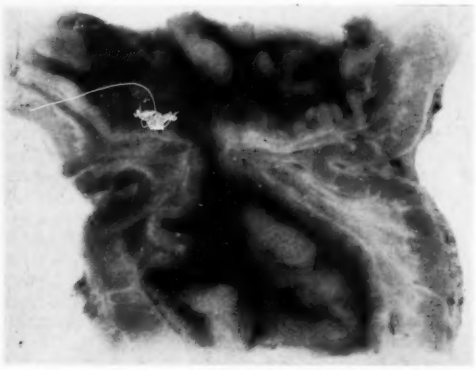

FIG. 389.—Stomach. Section of stricture tract, showing contraction of submucosal fibrous tissue and resultant drawing in of the mucosa and external muscle coats. (× 2.)

corrosives collected from the world literature up to 1950, and occasional cases have been reported since then, including 6 cases mentioned in this paper.

Many corrosive agents are known to cause strictures of the œsophagus and stomach, particularly acids and alkalis. In the majority of cases reported, acids have been taken, hydrochloric acid being the commonest one. Gastric strictures due to sulphuric acid have been reported less frequently, while on rare occasions acetic and nitric acids have been the causative agents. Very rarely strictures due to other corrosives have been recorded, e.g., formaldehyde and lysol (Schulenburg, 1941). It is not possible to obtain a completely accurate picture of the incidence of corrosive strictures, as on many occasions death has occurred in the early stages after the swallowing of strong acids and other substances before the onset of cicatrization. Gray and Holmes (1948) have observed that not as many people recover after having taken sulphuric acid as after hydrochloric acid, and thus there is a greater incidence of hydrochloric acid strictures. In most instances the corrosives are taken under circumstances of attempted suicide, but some authors have reported hydrochloric acid being taken in mistake for water or whisky.

One of the main features of interest in connexion with corrosive strictures of the stomach is the occur-

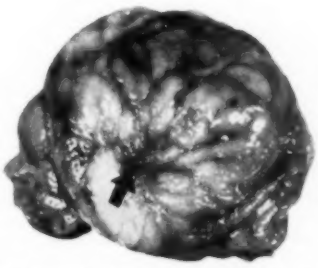

FIG. 388.—Stomach, showing proximal orifice of stricture.

rence of such a lesion, together with a complete sparing of the œsophagus when acid has been taken, as in the case reported. All authors have noted that stomach lesions predominate after acids, and that the œsophagus is predominantly affected after alkalis. The first such case described of a corrosive lesion of the stomach without involvement of the œsophagus was one by Robert (1828), sulphuric acid being the offending corrosive. It has been noted in the literature that, of recorded cases of lesions in the upper alimentary tract due to acids, the œsophagus escaped in 80 per cent, the main site of the stricture being the pylorus, gastric and œsophageal lesions occurring together in 20 per cent. Skapinker and Crawshaw (1954) have remarked that with alkalis both the œsophagus and the stomach are equally affected, the œsophagus bearing the brunt. Also in this respect Maggi and Meeroff (1953) stated that: "An acid material may leave the œsophagus unharmed, whereas it has never been known to escape injury when the material was alkaline—in the latter, the lesion may be exclusively œsophageal." Various explanations have been advanced to explain the differing effects of alkalis and acids, Strode and Dean (1950) saying that an ordinary concentration of acid has but a superficial scorching effect upon the squamous epithelium as it passes rapidly down the œsophagus, but the delicate columnar epithelium of the stomach is much more susceptible to the acid, and considerably more damage is done at this point. Skapinker and Crawshaw (1954) noted that caustic soda has a universal colliquative action irrespective of the tissue, and thus affects the œsophagus as well as the stomach. Quick neutralization of alkalis in the stomach was the main factor in minimizing their corrosive effects upon the latter, according to Gray and Holmes (1948). Paul (1951) attributed the scarcity of lesions in the œsophagus with acids to their rapid passage, and thus only a momentary contact with the mucosa of the pharynx and œsophagus. Severe pain from the acid dictates rapid swallowing in an effort to relieve pain, and thus the rapid passage down the œsophagus.

Observers agree that strictures in the stomach are usually confined to the terminal portion of the body and the antrum. It appears that the pylorus is rarely affected alone. The occasional case of hour-glass deformity is described and also duodenal lesions have been recorded rarely. Various observers have explained that the gastric lesions occur mainly in the prepyloric and pyloric regions because of the severe pre-antral spasm induced by the acid. The acid thus produces the maximum trauma where it is held up by the spasm. Testa (1938) demonstrated pre-antral spasm occurring in dogs after the ingestion of caustic soda and barium introduced by tube. Maggi and Meeroff (1953) also noted that other factors governing the site of the lesion in the stomach were the form and position of the organ and the position of the person at the moment of ingestion. There is more trauma with an empty stomach, and if any food is present it protects the greater curve mainly, the corrosive fluid flowing along Waldeyer's (1908) *Magenstrasse* on the lesser curve as far as the pylorus. Skapinker and Crawshaw (1954) noted the effect of this fluid in producing a pylorospasm, and contracture of the lesser curvature, and a short stomach. They recorded that, "In an empty contracted stomach the lesser curvature is vertical, and acid comes in contact with the whole gastric mucosa". However, Palmer and Scott (1949) argued that the theory of pre-antral spasm was not aided by gastroscopic findings. They noted that in no case of corrosive poisoning examined gastroscopically and reported was there a predilection of mucosal damage for the lesser curvature. On the contrary, the antrum and pylorus were often observed to be normal, the damage being situated more proximally. No alternate theory was offered, but they remarked that the possibility of increased sensitivity of the prepyloric mucosa to noxious agents should not be disregarded.

Other interesting features of the condition are: (*a*) The rapidity of onset of the stenosis; and (*b*) The presence of histamine-resistant achlorhydria. All recorded cases show that it is usually from four to six weeks between ingestion of the corrosive and the development of the stricture (three weeks in the case reported). The achlorhydria is said to be characteristic, and the observations of Katsch and Kalk (quoted by Maggi and Meeroff, 1953) are interesting. They noticed the reappearance of free hydrochloric acid after a time on two occasions in one patient who had tried to commit suicide by taking hydrochloric acid on each occasion.

Observers have called attention to several diagnostic features in obscure cases. Early post-prandial vomiting is described in corrosive strictures as distinct from the later vomiting generally occurring in the pyloric obstructions of carcinoma and peptic ulcer. Moynihan (1926) likened the antrum and pylorus in cases of corrosive strictures of the stomach to a normal uterus and cervix, the walls being thick and unyielding and the cavity small. Paul (1951) noted that over a corrosive lesion, the peritoneum retains its normal sheen, whereas it is thickened and scarred over a chronic ulcer. This retained sheen is well illustrated in *Fig.* 387.

A review of the literature shows that many methods have been tried in the treatment of the established lesion. Dilatation of the pylorus was used but the results were poor. Also the various forms of pyloroplasty such as pylorectomy, duodenosphincterectomy, sphincterectomy, gastro-duodenostomy, and pyloroduodenostomy have been tried on occasions, but owing to the unsuitability of the tissues the results have been unsatisfactory. Gastro-enterostomy has been employed in most cases recorded, and partial gastrectomy had only been used on three occasions up to 1948. Gray and Holmes (1948) treated their case of pyloric stenosis with partial gastrectomy (anterior Polya) and Strode and Dean (1950) treated their 2 cases, one being an hour-glass deformity, with partial gastrectomy. A case of extensive scarring and hour-glass deformity following the ingestion of a 5·25 per cent sodium hypochlorite preparation reported by Strange, Finneran, Schumacker, and Bowman (1951) required a total gastrectomy. A case of Maggi and Meeroff (1953) was treated with a subtotal Polya gastrectomy. It was necessary for Skapinker and Crawshaw (1954) to do a total gastrectomy on their case on account of the extensive involvement of the stomach.

There are various factors involved in the treatment of this condition, and, first of all, as is pointed out by Gray and Holmes (1948), the aim in treatment of the pyloric stenosis, irrespective of the cause, is to restore the normal passage of food and thus restore normal nutrition and fluid and electrolyte balance. These authors voice various possible objections to using gastro-enterostomy. First of all the tissues may be unsuitable. Then the advisability of leaving abnormal, scarred, chronically inflamed tissue behind is questioned. Occasionally elsewhere on epithelial surfaces in somewhat similar circumstances malignant lesions develop. Might they not develop here? Extensive squamous metaplasia was noted in one instance. Also the possibility of the development of a stomal ulcer is mentioned. One of the authors showed that stomal ulcers may develop in the absence of a definite ulcer diathesis, e.g., in cases subjected to the operation on the basis of an erroneous diagnosis of peptic ulcer. It was noted that scarring might lessen the tendency to a stomal ulcer. Skapinker and Crawshaw found that total gastrectomy was necessary in the presence of extensive scarring, gastro-enterostomy proving unsatisfactory in these circumstances. Paul admitted the possibility of the complication of stomal ulcer in gastro-enterostomy when done for this condition, but performed this operation on his three cases of pyloric stenosis because of the very low incidence of stomal ulcer in Ceylonese. In the light of the arguments voiced above, and on account of the localized nature of the lesion, partial gastrectomy was considered to be the operation of choice in the author's case.

SUMMARY

1. A case of corrosive stricture of the stomach without œsophageal involvement, caused by hydrochloric acid, is described.

2. The literature is reviewed and the incidence, circumstances, pathology, and treatment of corrosive stricture of the stomach are discussed.

I am indebted to Mr. S. Glaser for his assistance and permission to publish the case; Dr. R. L. Bishton

for the histological report; and Dr. P. Mann for helpful criticism. Also I wish to thank Mr. N. A. Swain for the photographs of the specimen and Mr. R. Marshall, of the Department of Photography, Cardiff Royal Infirmary, for the prints of the radiographs.

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INTRAMURAL GASTRIC TUMOURS

REPORT OF THREE CASES

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ALTHOUGH intramural tumours form only a small percentage of all gastric neoplasms they are of clinical importance. They are a cause of dyspepsia and, because of a tendency to ulcerate and bleed, chronic anæmia. In addition certain types, notably leiomyomas, not uncommonly become malignant; and occasionally the reticuloses may present as primary stomach tumours.

Palmer (1951), in an exhaustive review of the world literature, found reports of 1605 benign cases, classified as follows:—

Aberrant pancreatic tissue	215
Vascular tumours (angioma and endothelioma)	93
Lipomas	95
Schwannomas	181
Leiomyomas	610
Neurofibromas	41
Other fibromatous tumours (pure fibromas, myxofibromas, adenofibromas, etc.)	289
Cystic tumours (distinct from mucosal cysts and cystic degeneration in benign non-epithelial tumours)	81
	1605

Most of these tumours are submucous in site but occasionally they may be subserous or, less commonly, in the muscle layers and, except for aberrant pancreas which is nearly always in the prepyloric region, they may arise from any part of the organ. Apart from pancreatic and vascular tumours which are irregular in outline, they tend to be spherical, and sooner or later the mucosa over the summit ulcerates. This produces a deep pit in the tumour, with a distinctive X-ray appearance (*Fig.* 392).

Symptoms usually occur in middle age. Dyspepsia and pain are commonest, but occasionally the patient may present with hæmatemesis or melæna or with an unexplained anæmia (*Case* 2). Aberrant pancreas, by virtue of its prepyloric site, and other tumours also if they happen to arise from this part of the stomach, commonly cause symptoms of pyloric obstruction. Vascular tumours, as would be expected, often present with hæmorrhage. Very rarely large subserous tumours cause symptoms by pressing upon other viscera.

Diagnosis of an intramural gastric tumour can usually be made by barium-meal examination or by gastroscopy, but, apart from the rare occasions when a duct in aberrant pancreatic tissue may fill with barium, the type of lesion can only be determined by histology.

CASE REPORTS

Case 1.—Mrs. C. S., aged 49 years, was first seen in February, 1952. Twelve years before she had had a duodenal ulcer, which had resolved following medical

FIG. 390.—*Case* 1. Barium-meal examination showing a well-defined rounded tumour arising from the upper part of the greater curvature of the stomach. The mucosa appears intact.

treatment. During the past year she had suffered from dyspepsia thought to be caused by a recrudescence of the peptic ulcer. She had no actual pain, only a dull discomfort

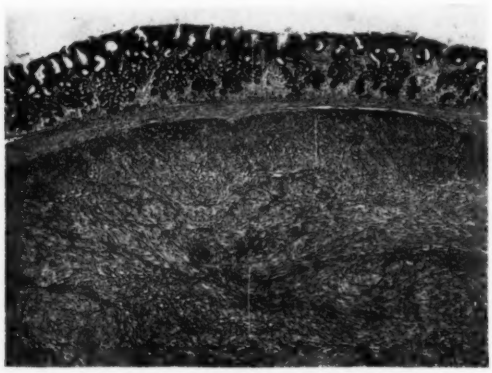

FIG. 391.—*Case* 1. Photomicrograph of specimen showing tumour composed of interlacing bundles of smooth-muscle cells deep to the muscularis mucosæ. (× 22·5.)

in the left hypochondrium, and nausea. She got some relief from drinking milk.

Nothing abnormal was found on clinical examination, but a barium meal (Dr. J. N. Pattinson) showed a well-defined rounded tumour in the upper part of the body of the stomach (*Fig.* 390).

At operation a spherical intramural tumour 1½ in. in diameter was found high up on the greater curvature. This was excised with a cuff of normal stomach and the defect sutured. Convalescence was uneventful and the patient lost her symptoms. She remains well at the time of writing.

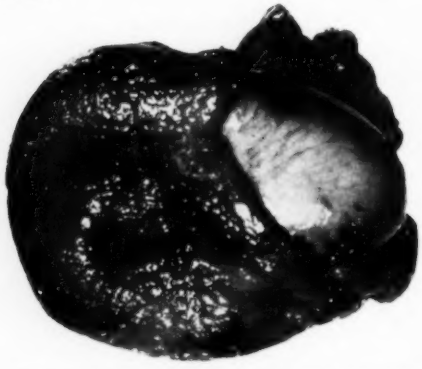

FIG. 393.—*Case* 2. Photograph of the specimen showing the cored-out ulcer in the otherwise intact mucosa, and the apparent encapsulation of the tumour. (× ½.)

Pathological examination showed a firm lobulated tumour in the wall of the stomach, covered by a thinned but intact mucosa. Histologically this was a typical leiomyoma (*Fig.* 391).

Case 2.—Mrs. D. P., aged 42 years. First seen in March, 1957, complaining of dyspepsia for the past five years. This consisted of epigastric pain and discomfort which came on a half to one hour after meals, with occasional nausea and vomiting. Symptoms were less severe when she adhered strictly to a gastric diet. She had also had two episodes of hæmatemesis in the past two years. A barium meal done three years ago was said to have shown a gastric ulcer. From the onset of her

FIG. 392.—*Case* 2. Barium-meal examination showing a filling defect on the greater curvature with smooth outlines and central ulcer pit.

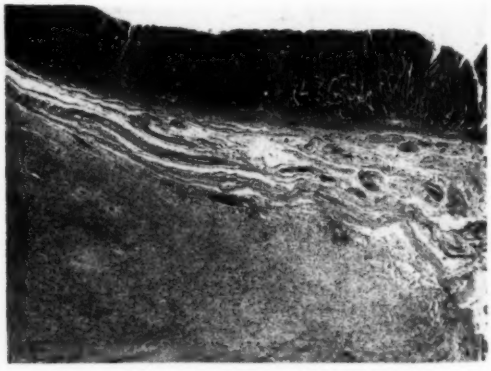

FIG. 394.—*Case* 2. Photomicrograph of specimen showing tumour composed of spindle-shaped cells in a myxomatous stroma in the submucosa of the stomach. (× 11·25.)

symptoms she had received several blood transfusions and had been on almost continuous iron therapy for persistent anæmia.

Clinically she was tender in the epigastrium and mildly anæmic. A barium meal (Dr. C. G. Whiteside) showed a filling defect on the middle of the greater curvature of the stomach with smooth outlines and a central ulcer crater (*Fig.* 392).

At operation a spherical intramural tumour 2 in. in diameter with a central ulcer was found and resected with

a wedge of normal stomach, the resulting defect being sutured. Convalescence was uneventful and her dyspepsia disappeared.

Pathological examination showed a firm, white, circumscribed tumour with ulcerated mucosa over it (*Fig.* 393). Histologically it was composed of fibrous tissue with myxomatous degeneration, suggestive of a fibromyxoma, or neurofibroma (*Fig.* 394).

Case 3.—E. E. B., male aged 59 years. First seen in June, 1957. He had had a Polya type partial gastrectomy in 1949 for duodenal ulcer. He remained well until 1951, when he began to suffer from bilious vomiting, usually

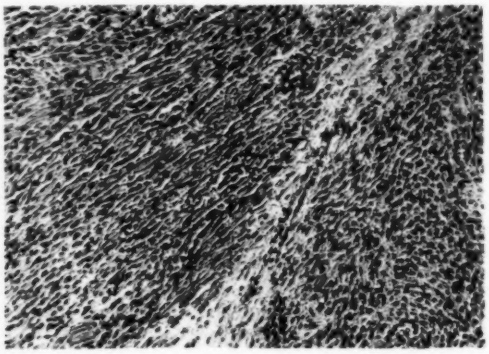

FIG. 395.—*Case* 3. Photomicrograph of specimen showing malignant smooth-muscle cells invading the stomach wall. (× 90.)

first thing in the morning. For the last seven months the bilious vomiting had stopped but it had been replaced by epigastric pain of increasing severity coming on about a quarter of an hour after meals. The pain was not relieved by alkalis. During this time he had lost 21 lb. in weight.

Clinical examination showed epigastric tenderness, smooth enlargement of the liver, and evidence of weight loss. A barium meal (Dr. C. G. Whiteside) showed a large filling defect in the fundus of the gastric remnant.

At operation a large irregular tumour was seen arising from the posterior wall of the fundus and infiltrating the posterior abdominal wall and the lower œsophagus. A secondary nodule was felt in the right lobe of the liver. A total gastrectomy and splenectomy was done with removal of the abdominal œsophagus, and a Roux-Y œsophagojejunostomy performed. Convalescence was satisfactory apart from the development of a left diaphragmatic pleurisy which responded to tetracycline.

Pathological examination showed a soft, polypoid, ulcerated tumour 3 in. in diameter arising from the fundus of the stomach remnant. Histologically this was a leiomyosarcoma which had invaded the peritoneum and the lower œsophagus (*Fig.* 395).

COMMENT

All three patients complained of dyspepsia, although only in *Case* 3 with a malignant lesion was pain a prominent symptom. In *Case* 2, with ulceration of the mucosa, hæmorrhage was an additional complication which produced prolonged anæmia as well as episodes of more severe blood-loss. *Case* 3 was, strictly speaking, inoperable, but a total gastrectomy was done for the relief of pain and to prevent subsequent obstruction.

Ulceration of the mucosa is a common finding in benign gastric tumours, and is probably caused by pressure necrosis in the same way in which the skin may ulcerate over a giant fibro-adenoma of the breast. This is no doubt related to the size of the underlying tumour. The ulcer is typically cored-out, giving rise to the appearance described as 'col utérin' by the French writers.

Most authors agree that the leiomyoma is the commonest benign gastric tumour, and the work of Meissner (1944) shows that small symptomless leiomyomas are much more common than is suggested by published case reports. In the course of 50 autopsies upon patients who had had no symptoms of dyspepsia he found small, smooth-muscle tumours in 23 stomachs, 40 separate tumours in all. These varied in size up to 0·7 cm. in diameter. In Meissner's laboratory there were 10 surgical specimens of leiomyoma and 11 of leiomyosarcoma, compared with nearly 700 carcinomas, an incidence of about 3 per cent. James (1956), from the Central Middlesex Hospital, reports that benign tumours accounted for about 2 per cent of all gastric neoplasms, and he quotes Ferguson, from the West Middlesex Hospital, who found 12 benign in 250 stomach tumours, an incidence of nearly 5 per cent.

Malignant change in these tumours is not always easy to detect histologically, but the presence of great variation in size and staining of the nuclei and of frequent mitotic figures are highly suggestive of malignancy. Rarely a smooth-muscle tumour of the alimentary tract which appears benign histologically may behave like a malignant neoplasm, invading locally and also metastasizing. For this reason simple enucleation is unwise. On the other hand, because they spread mainly by the blood-stream a wide dissection of the regional lymphatics is not warranted (Ackerman, 1953). Local removal with a reasonable margin of normal tissue is adequate unless at operation suspicion of malignancy is aroused by surrounding induration or by multiple areas of ulceration. Histology by frozen section at the time of operation may be helpful in cases of doubtful malignancy and in differentiating certain sarcomas from carcinoma.

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PUS COLLECTIONS IN HERNIAL SACS

AN UNUSUAL COMPLICATION OF GENERAL PERITONITIS

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It is well known that pus may collect in any peritoneal recess; such collections in the pelvis, paracolic gutters, or subphrenic spaces, accompanying or following a general peritonitis, are everyday occurrences. Much more rarely an empty hernial sac (which may be thought of merely as another recess of the peritoneal cavity) may similarly fill with pus.

We have operated on 5 patients with this complication over a period of twelve months; 3 examples occurred during the acute phase of a general peritonitis and 2 were late collections of pus after the main peritoneal infection had subsided.

This paper presents these 5 cases together with a review of the 27 examples which we have been able to collect from the literature.

It is, of course, not unusual for a hernia to become filled with pus as a result of the perforation of a contained viscus, particularly a gangrenous loop of strangulated bowel or an acutely inflamed appendix; such cases have been excluded from the present study.

CASE REPORTS

Case 1.—A. B. (R.I. 227941), a male aged 68 years, was admitted with a history of four days' generalized abdominal pain and vomiting, together with pain and swelling of his right inguinal hernia. This he had noticed for many years, but it had previously been painless and reducible.

On Examination.—He was obviously extremely ill. T. 98°, P. 120, B.P. 130/90. The abdomen was generally tender, distended, and silent, and a large, tense, irreducible and tender right indirect inguinal hernia was present.

A radiograph of the abdomen showed multiple dilated loops of small bowel with fluid levels. Exploration of the hernia (K. C.) revealed a large collection of pus in the sac, which was otherwise empty. As the pus was sucked away, more could be seen flowing down from the general peritoneal cavity. A paramedian incision was therefore made, a general peritonitis encountered, and a gangrenous perforated appendix removed. A swab of the pus grew *Bacterium coli*. He was given terramycin 250 mg. six-hourly, but died of bronchopneumonia on the third day; autopsy showed that the peritonitis had subsided.

Case 2.—P. G. (R.I. 239858), a man aged 68 years, gave a history of a right inguinal hernia first noticed in 1919 and still present in spite of two previous attempts at repair.

Forty-eight hours before admission he developed severe lower abdominal pain and vomiting. The pain became steadily worse and was accompanied by progressive swelling and pain in the hernia, which resisted his attempts to reduce it.

On Examination.—T. 98°, P. 80, R. 20, B.P. 140/95. There was generalized lower abdominal guarding and tenderness and the hernia was tender, tense, and irreducible. At operation (K. C.) the hernia was found to be distended with pus, but contained no abdominal viscus. The abdomen was then opened, revealing a general peritonitis due to a gangrenous, perforated appendix. Appendicectomy was performed. He was given a post-operative course of penicillin and streptomycin and made a satisfactory recovery.

Case 3.—S. S. (R.I. 223387), a housewife aged 73 years, had had an umbilical hernia for many years. Two years before admission she had a coronary thrombosis, and since that time had suffered from severe angina of effort. She was now admitted to hospital complaining of five days' severe central abdominal pain, vomiting, and distension.

On Examination.—She was severely ill, dyspnœic, cyanosed, and obese. T. 100°, P. 100, B.P. 110/80. The whole abdomen was tender, with marked muscle guarding, and there was a tense, painful, irreducible umbilical hernia present. Her general condition precluded the administration of a general anæsthetic and the hernia was therefore explored under local anæsthesia (H. E.). The sac was found to be tensely distended with pus, which could be seen welling up from the general peritoneal cavity. She was fit for no more than drainage of the peritoneum by means of a piece of corrugated rubber inserted through the umbilical incision. A course of penicillin and streptomycin was given and, to our surprise, she made a good recovery. The exact origin of the peritonitis remains unknown; the absence of previous abdominal symptoms and the fact that she was in fair health a year after operation suggests acute appendicitis.

Case 4.—J. P. (R.I. 230484), a man aged 63 years, was initially admitted with a perforated duodenal ulcer. This was repaired, and a course of penicillin and streptomycin given. Recovery was initially satisfactory, but on the sixth post-operative day he found that his left inguinal hernia, which had been present for many years, had now become painful and tense. He was found on examination to have a temperature of 99°; the hernia was tender and irreducible, with considerable redness and heat of the overlying skin. Operation (H. E.) revealed an indirect inguinal hernia, the sac of which was distended with pus but contained no viscus. The sac was excised and the hernia repaired with catgut. A further course of penicillin and streptomycin was given and he made a satisfactory recovery. Culture of the pus was sterile.

Case 5.—G. C. (R.I. 95520), a housewife aged 50 years, developed a generalized biliary peritonitis following removal of a T-tube drain ten days after a cholecystectomy and exploration of the common bile-duct. The abdomen was re-opened, the liver bed drained, and she was given a course of penicillin and streptomycin. She made satisfactory progress for seven days, but she then noticed a painful lump in the left groin. Her temperature was 100° and examination revealed a tender, irreducible, indirect left inguinal hernia. She had not previously noticed a rupture, nor had this been evident at examination on her admission to hospital.

At operation (H. E.) the hernia was found to be distended with pus. The sac was excised and a five-day course of sulphadiazine given. Recovery was uneventful.

REVIEW OF THE LITERATURE AND DISCUSSION

A review of the available literature has revealed only 27 other examples of hernial sacs distending with pus following a general peritonitis. These cases, together with the 5 patients here recorded, are summarized in the table.

Table I.

No.	Author	Year	Sex	Age	Site	Source of Peritonitis	Clinical Features and Treatment	Outcome
1	Zuckerkandl	1891	M.	55	R.I.H.	Appendicitis	Six days' painful irreducible hernia. Sac drained; contained pus only. Perforated appendix which was lying above the sac was not removed	Recovery
2	Langton	1895	M.	62	R.I.H.	?	Five days' painful irreducible hernia. Sac drained; contained pus only	Recovery
3	Naumann	1898	F.	42	R.F.H.	Appendicitis	One day's abdominal pain and painful irreducible hernia. Walls of sac thickened and inflamed; sac drained. Abdominal pain persisted. Removal of acutely inflamed appendix the following day	Recovery
4	Nakashian	1898	M.	27	R.I.H.	?	Ten days' abdominal pain. Five days' painful irreducible hernia. Sac drained; contained one pint of pus	Recovery
5	Spellisy	1906	M.	23	R.I.H.	Probably appendicitis	Mental defective. Presented with painful irreducible hernia and mass in R.I.F. Sac contained four pints of pus. No further history given	Recovery
6	Sewell	1906	M.	?	R.I.H.	?	Five days' pain in R.I.F. and painful irreducible hernia. Sac drained; contained pus only. No improvement. Three days later, laparotomy—distended gut, no obvious obstruction. Died twelve hours later. P.M.: general peritonitis in lower abdomen but no primary cause found, appendix normal	Death
7	Clairmont	1909	M.	35	R.I.H.	Appendicitis	Died after two days' abdominal pain and painful irreducible hernia. P.M.: perforated appendix; general peritonitis; sac contained pus only	Death
8	Clairmont	1909	F.	27	R.I.H.	Right pyosalpinx	Two days' painful irreducible hernia. Sac contained pus only. Laparotomy and right salpingectomy	Recovery
9	Clairmont	1909	M.	34	R.I.H.	Appendicitis	Four days' right-sided abdominal pain with painful irreducible hernia. At operation, walls of sac thickened and inflamed. Patient died. P.M.: perforated appendix with general peritonitis	Death
10	Barker	1912	F.	53	R.F.H.	Appendicitis	Ten days' painful irreducible hernia and mass in R.I.F. Sac drained; contained pus only. Ten days later, appendicectomy	Recovery
11	Barker	1912	F.	62	R.I.H.	Probably appendicitis	Nineteen days' painful irreducible hernia. Sac drained; contained pus only. Main abscess in region of appendix	Recovery
12	Lenormant	1914	M.	65	Epigastric	Perforated gastric ulcer	Nine hours' severe abdominal pain. Irreducible epigastric hernia opened and found to contain soup. Laparotomy and repair of perforated gastric ulcer	Recovery
13	Bennett	1919	M.	?	R.I.H.	Appendicitis	One day's pain in R.I.F. with painful irreducible hernia. Sac contained pus only. Laparotomy and removal of gangrenous appendix	Recovery
14	Madlener	1926	F.	48	R.F.H.	?	Sac drained; contained pus only. No length of history given	Recovery
15	Kincaid	1926	M.	2 wk.	R.I.H.	Pneumococcal peritonitis	Admitted with irreducible hernia and died soon after. P.M.: pus in sac and general peritonitis	Death
16	Oliva	1926	M.	69	L.I.H.	?	Four days' abdominal pain. One day's painful irreducible hernia. Sac drained; contained pus only	Recovery
17	Miller	1930	M.	74	R.F.H.	Appendicitis	Three days' painful irreducible hernia with generalized abdominal pain. Sac contained pus only. Laparotomy and removal of perforated appendix	Recovery
18	Aigrot	1931	F.	30	L.F.H.	Appendicitis	Painful irreducible hernia three days after appendicectomy. Sac drained; contained pus only	Recovery
19	Aigrot	1931	M.	50	R.I.H.	Appendicitis	Four days' abdominal pain with painful irreducible hernia. Sac contained pus only. Laparotomy and removal of gangrenous appendix	Recovery
20	Aigrot	1931	M.	?	R.F.H.	Appendicitis	Four days' abdominal pain with painful irreducible hernia. Sac contained pus only. Laparotomy and removal of acutely inflamed appendix	Recovery
21	Aigrot	1931	M.	50	R.I.H.	Perforated gastric ulcer	Five days' abdominal pain; diagnosed as perforated peptic ulcer. Refused operation. Four days later developed swelling of right inguinal hernia. Sac contained pus only. Laparotomy and repair of perforation	Recovery
22	Muller	1932	F.	44	L.F.H.	?	Six days' abdominal pain. Three days' painful irreducible hernia. Sac drained; contained pus only	Recovery

Table I. (continued)

No.	Author	Year	Sex	Age	Site	Source of Peritonitis	Clinical Features and Treatment	Outcome
23	Harris	1936	M.	15	R.I.H.	Appendicitis	Painful irreducible hernia appeared five days after appendicectomy. Drainage of sac and orchidectomy	Recovery
24	de Simone	1937	M.	75	R.I.H.	?	Four days' painful irreducible hernia. Sac drained; contained pus only	Recovery
25	de Simone	1937	F.	51	L.F.H.	?	Two weeks' painful irreducible hernia. Sac drained; contained pus only	Recovery
26	de Simone	1937	M.	12	R.I.H.	?	Painful irreducible hernia for 'few days'. Sac drained; contained pus only	Recovery
27	de Simone	1937	M.	65	R.I.H.	Appendicitis	Six days' pain in abdomen. Four days' painful irreducible hernia. Sac drained; contained pus only. Three days later developed mass in R.I.F. and gangrenous appendix removed	Recovery
28	Present authors		M.	68	R.I.H.	Appendicitis	Four days' pain in abdomen and painful irreducible hernia. Sac contained pus only. Laparotomy and removal of perforated appendix	Death
29	Present authors		M.	68	R.I.H.	Appendicitis	Two days' pain in abdomen and painful irreducible hernia. Sac contained pus only. Laparotomy and removal of perforated appendix	Recovery
30	Present authors		F.	73	Umbilical	?	Five days' abdominal pain and painful irreducible hernia. Sac drained; contained pus only	Recovery
31	Present authors		M.	63	L.I.H.	Perforated duodenal ulcer	Painful irreducible hernia six days after repair of perforated duodenal ulcer. Sac contained pus only	Recovery
32	Present authors		F.	50	L.I.H.	Biliary leak following removal of C.B.D. drain	Painful irreducible hernia seven days after general peritonitis following removal of T-tube from common bile-duct. Sac contained pus only	Recovery

Age and Sex Incidence.—No age appears exempt from this complication; it has been recorded in a baby of two weeks and in several patients in their seventies. Twenty-two of the patients were male and 10 female, the males predominating, no doubt, because of the higher incidence of inguinal hernia in this sex.

Type of Hernia involved.—Of the 32 herniæ involved, 19 were right inguinal, 5 right femoral, 3 left inguinal, 3 left femoral, 1 epigastric, and 1 umbilical.

Aetiology of the Peritonitis.—Acute appendicitis with perforation accounted for 16 examples, 3 occurred after perforated peptic ulcers, and 1 each followed a pneumococcal peritonitis, an acute pyosalpinx, and a biliary leak after removal of a drain from the common bile-duct. In no less than 10 cases, however, the aetiology of the general peritonitis remained undetermined; in these, drainage of the sac alone was carried out and there was only 1 death.

Since acute appendicitis is the commonest cause of general peritonitis, one might assume that the majority of the 10 examples were, in fact, due to this. However, in the 1 case where death followed simple drainage of the sac, autopsy failed to reveal the primary cause of the peritonitis.

The Immediate and Delayed Groups.—The patients in this study may be classified into two groups, the immediate and the delayed. In the *immediate group* (27 cases) distension of the hernial sac occurred during the acute phase of the general peritonitis. It is possible that some contamination of the sac occurs in many patients with general peritonitis who have a coexisting hernia; in fact, while preparing this paper, we have seen 3 patients with general peritonitis in each of whom slight swelling and definite tenderness of an associated inguinal hernia were found. In spite of this contamination, definite distension of the hernia with pus is unusual. It would appear that the factors favourable to the development of the complication are a large amount of fluid present in the peritoneal cavity and delay in treatment of the peritonitis; the average duration of symptoms in the cases reported in the literature was four and a half days, and in our own 3 cases was two, four, and five days.

In the delayed group (5 cases) contamination of the hernial sac no doubt occurred during the acute phase of the peritonitis, but with no local signs or symptoms. Three to nine days after the general peritoneal infection had subsided, abscess formation occurred within the sac in much the same way as a subphrenic or pelvic abscess might form. All five cases recovered after drainage.

Diagnosis.—Every patient in this series was incorrectly diagnosed pre-operatively as having a strangulated hernia. It might appear surprising that difficulty should have arisen in differentiating between a peritonitis and a strangulated hernia, but the presence of a painful irreducible swelling, about which the patient complains bitterly, makes it difficult for the surgeon to entertain any other diagnosis. Most of these patients, as we have already noted, had had symptoms for several days before reaching hospital, and it is notoriously easy to interpret the pain and distension of a late peritonitis as being due to an obstruction.

Occasionally a clue to correct diagnosis would have been the history of abdominal pain clearly

preceding the hernial swelling, but this occurred in only 4 of the 27 patients in the 'immediate' group.

Diagnosis in the 'delayed' group, in retrospect, should have been relatively simple if it were not for the rarity of this condition. An irreducible hernia, accompanied by pyrexia, occurring in a patient convalescing from a general peritonitis, should suggest that a collection of pus, rather than an abdominal viscus, constitutes the contents of the sac.

SUMMARY

1. A syndrome is described in which the empty hernial sac, in its role of a peritoneal recess, becomes distended with pus during or after a general peritonitis.

2. Five new cases are presented, together with 27 others collected from the literature.

We would like to thank Mr. D. A. Abernethy and Mr. A. Elliot-Smith for permission to publish details of these patients, who were admitted to the Radcliffe Infirmary under their care.

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SEVERE MELÆNA DUE TO A LEIOMYOMA OF THE DUODENUM

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SEVERE melæna in adults is so frequently a complication of peptic ulceration or acute gastroduodenal erosion that the rare causes of the condition are liable to be forgotten. Smooth-muscle tumours of the small intestine are not common, but they have a very pronounced tendency to bleed, and, as emphasized by Gordon-Taylor (1944), the bleeding may at times be severe and even fatal.

The following case is reported as a reminder of this rare but important source of intestinal hæmorrhage.

CASE REPORT

Mr. L. S., aged 51 years, was admitted to Westminster Hospital as an emergency on Sept. 3, 1957. For the previous five days he had felt weak and faint, and had passed several melæna stools. For many years he had been subject to slight flatulent dyspepsia. Eighteen months previously he had been admitted to another hospital with an iron-deficiency anæmia. Barium meal at that time revealed no abnormality, and his anæmia was attributed to bleeding piles. Nine months later he was re-admitted to the same hospital following an attack of melæna, and a barium meal on this occasion showed some narrowing of the duodenal cap suggestive of old ulceration. He was given medical treatment as an out-patient. Despite iron therapy he remained anæmic up to the time when further melæna necessitated his admission to Westminster Hospital.

ON EXAMINATION.—The patient was very pale, and felt faint on sitting up. He was not shocked. Pulse 90/min. B.P. 105/70. There was slight tenderness in the epigastrium, but no mass was palpable in the abdomen. Blood examination revealed hæmoglobin 37 per cent = 5·5 g. per 100 ml. Blood transfusion was commenced, but despite this the blood-pressure fell during the 24 hours after admission, and it appeared that bleeding was continuing. Laparotomy was therefore advised.

AT OPERATION (Sept. 4).—Under general anæsthesia (Dr. R. Wise) the abdomen was opened through an upper midline incision, later extended transversely across the left rectus muscle. Altered blood could be seen in the small bowel, but there was no external evidence of peptic ulceration or other lesion in the stomach or first part of the duodenum. At this stage a tense, reddish, lobulated tumour was discovered in the retroperitoneal tissues high up on the left side of the abdomen, in front of the left kidney, and below the body of the pancreas. The tumour

FIG. 396.—Photograph of the tumour as seen at operation after mobilization of the duodenum.

was not invading surrounding structures and was freed without much difficulty. It then became apparent that it was attached to and arising from the left side of the fourth part of the duodenum, and that although the main mass of the tumour projected in a bilobular manner outside the bowel wall there was also a small rounded portion projecting into the lumen. There were no enlarged lymph-nodes to be seen, and the remainder of the small bowel was normal. No secondary deposits were felt in the liver or remainder of the peritoneal cavity. From its macroscopical appearance the lesion was thought to be a leiomyosarcoma.

After mobilization of the third and fourth parts of the duodenum and of the duodenojejunal flexure (*Fig.* 396) a 5-in. segment of bowel, with the tumour near its centre, was resected, and end-to-end duodenojejunostomy performed. The abdomen was closed without drainage.

The early post-operative course was uneventful, but on the eighth day abdominal pain and vomiting developed, and this was thought to be due to a partial high intestinal obstruction. Temporary improvement occurred with gastric aspiration and intravenous fluids, but recurrence of obstructive symptoms necessitated re-exploration of the abdomen on Sept. 22. The first loop of jejunum had slipped up behind the transverse mesocolon and become adherent in this position. It could not readily be freed, and an anterior gastrojejunostomy was deemed the wisest course. Following this procedure his progress was uneventful and he was discharged from hospital on Oct. 15. He has subsequently remained well.

FIG. 397.—Photograph of the resected specimen showing large lobulated subserous leiomyoma. (× ⅔.)

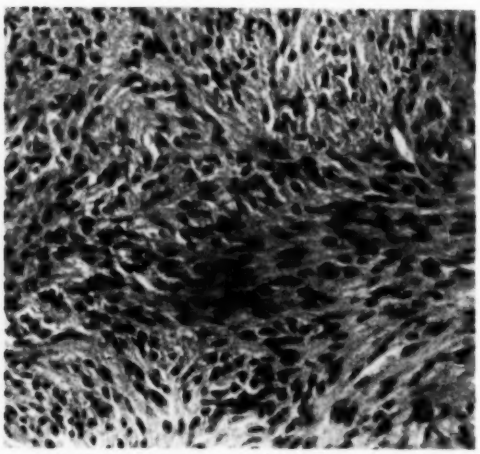

FIG. 399.—Photomicrograph of the tumour. (× 150.)

THE SPECIMEN.—

"*Macroscopy* (*Figs.* 397, 398): The specimen consists of 4 in. of small bowel to which is attached a sausage-shaped tumour 1½ in. thick and 4½ in. long. It is covered by peritoneum and is attached to the antimesenteric border of the bowel by a pedicle 1½ in. in diameter. A rounded nodule 1 in. in diameter projects from this pedicle into the lumen of the bowel. The surface of this nodule is mainly smooth, but there is an irregular ulcer on its summit. When cut across, the main tumour is white and rubbery in its centre portion, contains a large cyst at one end and ageing blood-clot at the other."

"*Histology* (*Fig.* 399).—The tumour consists of spindle-shaped cells compatible with smooth-muscle origin. It is well demarcated and does not invade the muscularis mucosæ of the duodenum. Some parts are degenerate and very vascular, leading to localized hæmorrhage. The uniformity of the cells and the whorled arrangement support the diagnosis of a benign leiomyoma."

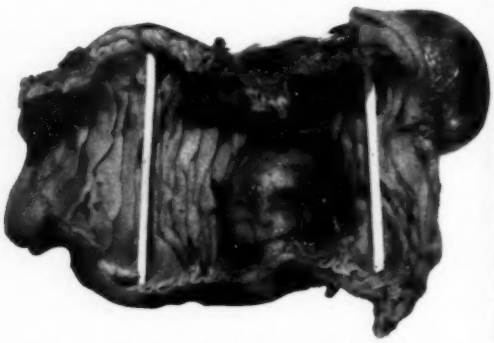

FIG. 398.—Photograph showing the intraluminal projection of the tumour with ulceration on its summit. (× ⅔.)

DISCUSSION

Leiomyomata of the small bowel have been well reviewed by Golden and Stout (1941) and by Starr and Dockerty (1955). The latter collected 230 cases from the literature, and the duodenum was the site of the tumour in 20 per cent.

Pathology.—Whether benign or malignant, these tumours have a marked tendency to grow predominantly as lobulated subserous projections. This is well exemplified in the present case, in which there was also a much smaller intraluminal protrusion. Bulky subserous tumours are extremely liable to central necrosis, and cavitation may occur as a result of discharge of necrotic tumour tissue into the lumen of the bowel. Norris Smith (1937) considered that the firm walls of such a cavity and the free drainage into the lumen were the main factors in preventing the arrest of hæmorrhage from these vascular tumours. In the present case, although the tumour showed cystic degeneration and hæmorrhage, cavitation had not occurred, and the bleeding had arisen from superficial ulceration of the intraluminal projection.

More than half the published cases of smooth-muscle tumours of the small bowel have been described as malignant, though the degree of malignancy is difficult to assess on histological criteria, and most malignant leiomyomata metastasize slowly. Starr and Dockerty (1955) regard the size of the tumour as a useful guide to its subsequent behaviour. The tumour in the case here reported was larger than any of the 35 benign examples in their series of 76 cases, and its macroscopical appearance suggested

a malignant lesion, though there were no obvious metastases.

Diagnosis.—In the present case recurrent melæna, with intervening anæmia, was the significant clinical feature, and this is the commonest mode of presentation of these tumours. A palpable mass is present in some 30 per cent of cases, the majority of these being malignant. Intestinal obstruction is unusual, and occurs mainly as a result of intussusception complicating a submucous tumour.

Radiography is of limited value in diagnosis, partly on account of the difficulty of obtaining good pictures of the small intestine in the absence of an obstructive lesion, and partly because of the tendency of these tumours to extend outwards into the peritoneal cavity rather than into the lumen. In the present case barium meals on three separate occasions had not been helpful, an added difficulty being that the site of origin of the tumour lay concealed behind the stomach.

In many cases the diagnosis will not be made until recurrent bleeding episodes indicate the necessity for laparotomy. Tumours arising in the jejunum and ileum will then readily be discovered. In the present case the lesion arose from the fourth part of the duodenum, and extended retroperitoneally, and had it not been a relatively large tumour it might easily have been missed. The necessity for careful palpation of the whole duodenum at operation for unexplained gastro-intestinal hæmorrhage is perhaps insufficiently stressed in the text-books.

Treatment.—The resection of smooth-muscle tumours arising in jejunum or ileum is usually straightforward, but where the duodenum is the site of origin the difficulties may be considerable. Weinstein and Roberts (1953) reviewed 28 cases of leiomyosarcomata of the duodenum in the literature. Resection of the lesion was performed in 18 of these and there were 6 post-operative deaths, a mortality of 33 per cent. This high mortality is doubtless due in considerable part to the proximity of the pancreas and other important structures. In the present case it was possible to mobilize the tumour and that part of the duodenum lying to the left of the superior mesenteric vessels. A satisfactory resection and end-to-end anastomosis was then possible without much difficulty.

SUMMARY

A case is reported of recurrent melæna due to a large leiomyoma of the duodenum. Resection was successfully performed.

I wish to thank Mr. E. Stanley Lee and Dr. R. I. S. Bayliss for permission to publish this report, and for their helpful advice. My thanks are also due to Mr. Lee and to Dr. P. Hansell for the photographs; to Dr. D. H. Mackenzie for the photomicrograph; and to Dr. A. D. Morgan for the pathological report.

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LEIOMYOSARCOMA OF CERVICAL STUMP FOLLOWING SUBTOTAL HYSTERECTOMY

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THE important and well-recognized contra-indication to subtotal hysterectomy is the possibility of a carcinoma developing in the remaining cervix. It is not generally appreciated that a leiomyosarcoma may occur in the cervical stump. The following case history is interesting in this respect.

CASE REPORT

Mrs. M. G., a housewife, aged 42 years, had a subtotal hysterectomy for a fibroid uterus at another hospital in 1948. The histological picture at this time was typical of fibromyoma. By November, 1953, five years later, another tumour had appeared in the left iliac fossa and pelvis and at operation a mass in the region of the left ovary and cervical stump was removed: histologically this tumour was a leiomyosarcoma with varying cellularity and of low-grade malignancy (*Fig.* 400).

For two years the patient was well, with no evidence of recurrence, but in May, 1956, another mass was found rising out of the pelvis on the right side of the abdomen and occupying the pouch of Douglas. Surgery was thought to be contra-indicated and she was given a course of high-voltage therapy (250 kV.), a tumour dose of 4200 r being administered in thirty-eight days. Following therapy the mass did not regress; on the contrary, it increased rapidly in size. Treatment was discontinued in October, 1956, and eleven months later the tumour occupied almost the

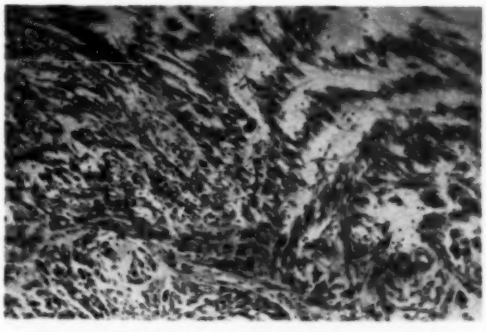

FIG. 400.—Tumour of cervical stump removed in 1953. A leiomyosarcoma of low-grade malignancy. H. & E. (× 54.)

whole of the abdomen and pelvis and was compared to a 30-week pregnancy; it was embarrassing respiration, the patient felt extremely uncomfortable, and she demanded operation. A chest radiograph showed no pulmonary metastases and an intravenous pyelogram was normal apart from displacement of the right ureter and there were no bony pelvic metastases.

On Sept. 25, 1957, the tumour was exposed through a long right paramedian incision. It was retroperitoneal

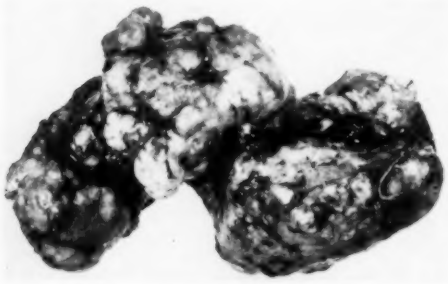

FIG. 401.—Recurrent tumour weighing 6 lb. 6 oz. removed in 1957, showing two well-encapsulated lobulated masses joined by a narrow isthmus.

and the pelvic extension of the tumour burrowed into the bladder wall without ulcerating the mucosa, and numerous coils of small intestine were adherent to the mass. The intestine was freed, a partial cystectomy performed, and the tumour delivered intact. The bladder was sutured in two layers and the main incision with catgut, and thread for the skin. Following the operation she made an uneventful recovery and when seen seven weeks later she was in good health, free from urinary symptoms, and had gained 9 lb. in weight.

The tumour removed at operation weighed 6 lb. 6 oz. (2880 g.) and was in two lobulated masses (abdominal and pelvic), measuring $20 \times 9 \times 7$ cm. and $17 \times 10 \times 10$ cm., joined by a narrow isthmus of fibrous tissue (*Fig.* 401). The cut surface showed the characteristic appearance of a fibromyomatous tumour with large areas of degenerative change. Sections from various parts of the tumour showed "the general structure of a leiomyoma, but the cellularity is greater than is usually seen and the cell nuclei show bizarre giant forms, rather numerous mitotic figures and marked hyperchromatism—a leiomyosarcoma of definitely low-grade malignancy" (*Fig.* 402). The presence of these cell nuclei with bizarre giant forms was thought to indicate irradiation changes in the tumour. A careful scrutiny of the histological features of the tumour removed in 1953 (*Fig.* 400), however, reveals the presence of similar cells. These abnormal giant-cell nuclei are therefore regarded as an inherent cytological feature of these tumours which corresponds to the giant-cell type of sarcoma described by Novak (1952).

The patient was re-admitted to the Samaritan Hospital for Women in November, 1958, with a further tumour mass in the pelvis. At laparotomy two large and three smaller tumour recurrences were found in the pelvis, and one of these was adherent to the small bowel and bladder. It was not possible to remove the recurrences completely. The histological picture of these tumours was similar to that described in this paper.

DISCUSSION

Novak (1952) described a case who lived five years after subtotal hysterectomy for a fibroid uterus and in this period had three operations for tumour recurrence. Histologically the last tumour was a polymorphic sarcoma, but the other two recurrences showed no evidence of malignancy.

The two interesting features of the tumour described in this paper are its slow rate of growth and its complete insensitivity to irradiation. Subtotal hysterectomy was performed in 1948 for uterine fibroids. A leiomyosarcoma of the cervical stump was removed five years later in 1953 and

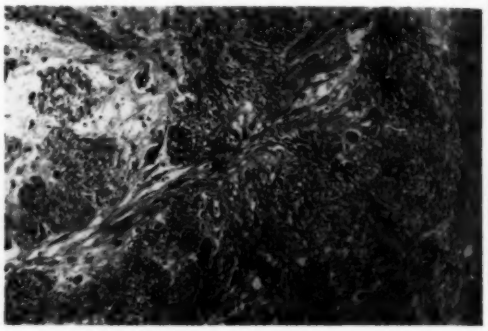

FIG. 402.—Leiomyosarcoma removed in 1957. The cell nuclei show bizarre giant forms, numerous mitotic figures, and marked hyperchromatism. H. and E. (× 54.)

recurrences in 1957 and 1958. The prognosis is, therefore, comparatively good as the patient has already lived five years since the tumour was first treated and in this time has had recurrences removed surgically.

The growth is completely insensitive to irradiation. Following thirty-two days' treatment on the 250-kV. machine there was no decrease in tumour size and no retardation of the rate of growth of the tumour. Surgery seems to offer the only hope of eradicating the disease, and in view of the encapsulated nature of the tumour its removal did not offer any great technical difficulty. It would perhaps, in retrospect, have been wiser to attempt surgical removal at an earlier date before the tumour had attained such forbidding dimensions.

SUMMARY

A case of leiomyosarcoma of the cervix following subtotal hysterectomy is presented. The possibility of such a tumour developing in the cervical stump is stressed and should be cited as one of the contra-indications to this operation in all cases where hysterectomy is planned. The operation of choice is a total hysterectomy. The slow rate of growth of the tumour and its complete insensitivity to radiotherapy is noted.

I am indebted to Mr. Douglas MacLeod for permission to publish this case report. My thanks are also due to Dr. N. F. C. Gowing for the microphotographs and pathological reports, and to the Medical Photography Department for *Fig.* 401.

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A CASE OF MYXOMA OF THE LEFT ATRIUM WITH PERIPHERAL ARTERIAL EMBOLI

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PRIMARY heart tumours are rare; figures quoted for their frequency at autopsy range from 0·0017 per cent (Straus and Merliss, 1945) to 0·61 per cent (Lymburner, 1934). The commonest of these is the so-called myxoma which may rarely throw off tumour emboli (Gorlitzer, 1934; Young and Hunter, 1947; Brewin, 1948; Block, Parker, and Edwards, 1952; Gleason, 1955). Since these neoplasms can now be accurately diagnosed by angiocardiography (Goldberg, Glenn, Dotter, and Steinberg, 1952; Bahnson and Newman, 1953; Steinberg, Dotter, and Glenn, 1953) and successfully removed (Crafoord, 1954, quoted by Brock, 1956; Scannell, Brewster, and Bland, 1956; Chin and Ross, 1957), myxoma of the heart should be borne in mind as a possible source of peripheral embolism.

CASE REPORT

An obese woman aged 70 years was admitted to the Royal Infirmary, Bradford on Aug. 12, 1956. While seated, one hour prior to admission, she had noticed the sudden onset of paræsthesia in the legs and had been unable to rise to her feet. She was very distressed by pain distributed over the lower lumbar region and said her legs felt numb. For two years previously she had suffered from frequent attacks of 'bronchitis' and dyspnœa,

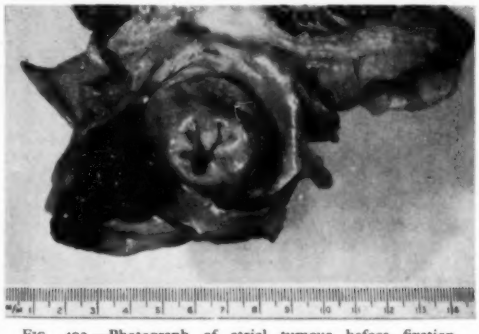

FIG. 403.—Photograph of atrial tumour before fixation, showing gelatinous appearance.

although there had apparently been no evidence of heart failure. Previous to this she had always been well and there was no history of angina or intermittent claudication.

ON EXAMINATION.— Her blood-pressure was 100/70 and the pulse regular but of poor volume. Heart-sounds were distant, with no audible murmurs. There was no dyspnœa and on auscultation breath-sounds were vesicular with no adventitious sounds. The abdomen relaxed well and no abnormal mass viscus or pulsation could be felt. The legs were appreciably cooler than the rest of the body, mottled in colour, and with a cyanotic tinge. There was no œdema. All sensation was absent, except deep pain in the upper thighs. Skin and tendon reflexes were absent, and no arterial pulsation could be perceived distal to and including the groins. A radiograph of the chest disclosed no abnormality in the lung fields or cardiac shadow, and a soft-tissue film of the abdomen did not define the aorta or any related mass.

A diagnosis of a thrombo-embolic episode involving the bifurcation of the aorta was made. No evidence could be adduced as to the source of the embolus. An alternative diagnosis of a dissecting aneurysm was considered less likely.

AT OPERATION.— One hour after admission the aorta was exposed under general anæsthesia through a long

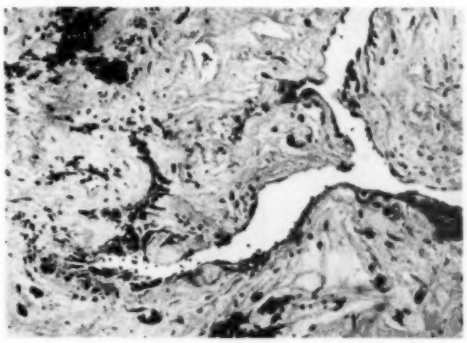

FIG. 404.—Section showing the matrix of pale eosinophilic material infiltrated with lymphocytes and stellate cells. A few scattered red cells are present. H. and E. (× 150.)

lower left paramedian incision. Pulsation in the vessel was seen to cease between the origin of the renal and inferior mesenteric arteries. After occluding the common iliac arteries by means of Blalock pulmonary artery clamps the distended lower end of the aorta was dissected proximally until good pulsation was evident and a Pott's coarctation clamp applied. An incision was made in the aorta extending into the left common iliac artery and pink tenacious glistening jelly-like material was removed, the removal being facilitated by intermittently releasing the Pott's clamp. The material was recognized by the operator as being unlike normal blood-clot but its true significance was not appreciated at the time. Upon releasing the Blalock clamps good retrograde bleeding occurred. The isolated segment of vessels was washed out with heparin solution and the incision sutured. The patient was then heparinized and 50 mg. of papaverine hydrochloride was injected into each common iliac artery, after which good femoral pulsation could be felt on each side. A bilateral sympathetic ganglionectomy was carried out before the peritoneum was closed over the aorta and the abdomen closed. The patient received one pint of blood during the operation and returned to the ward in a satisfactory condition with the blood-pressure at the pre-operative level.

Her condition remained very satisfactory until four hours after the operation when she suddenly collapsed and died. No clinical cause could be found for this change in her condition, but in the light of the autopsy findings

it may have coincided with blockage of the mitral valve or a further cerebral embolus.

AT AUTOPSY.—The heart was moderately enlarged (weight 375 g.) owing to slight hypertrophy of the left ventricle. There was no right ventricular hypertrophy. In the left atrium an irregular lobulated tumour, measuring approximately 5 by 3 cm., was attached to the inter-atrial wall by a slender pedicle close to the foramen ovale. It was very soft and gelatinous in consistency (*Fig.* 403) and of pale red colour throughout. It showed no obvious pressure marks to indicate long-standing impaction in the mitral valve orifice, but was sufficiently large and mobile to have caused intermittent obstruction. The heart was otherwise normal, with little evidence of coronary atheroma and no sign of valvular disease.

In the abdominal aorta the recent incision was in good order and there was no thrombosis at the operation site. No embolic fragments remained in the lower part of the aorta, but the left renal artery was completely occluded by tissue similar to that in the left atrial mass and another small embolus was attached to an atheromatous plaque 5 cm. proximal to the origins of the renal arteries. In the brain there were two small areas of softening present in the right cerebral cortex, although no embolic material could be found in the main cerebral arteries and branches.

Histological examination of the left atrial tumour showed the appearances usually described in myxoma of the heart—namely, a matrix of eosinophilic fibrillary material infiltrated with lymphocytes and macrophages and containing solid clumps, and acinar masses of polyhedral cells with occasional solitary stellate cells (*Fig.* 404). In sections stained by the muci-carmine method no mucin could be detected. The emboli recovered at operation and at autopsy showed similar appearances.

DISCUSSION

Concerning the pathology, there is still some doubt as to the true nature of myxoma of the heart. In the most comprehensive review of the subject Pritchard (1951) weighed the evidence as to whether the tumour was a true neoplasm or derived from organized thrombus and concludes, "aside from bearing a superficial similarity to some thrombi there is little to indicate that they are thrombi or arise from them and the bulk of evidence indicates that they are true neoplasms. Mechanical factors are probably responsible for the frequent myxoid character of these connective tissue tumours."

The clinical picture of myxoma of the heart is very varied and Fawcett and Ward (1939) describe seven of the commoner modes of presentation. The tumour can occur at any age and there are references in the literature to cases occurring even in childhood (Young and Hunter, 1947; Gleason, 1955). Emboli may become detached from clot on the surface of the tumour (Weinstein and Arata, 1949; Brown, 1946) as well as from the tumour itself. Since embolic events may be repeated and minor in nature, subacute bacterial endocarditis can be closely simulated, particularly since the tumour may produce symptoms and signs resembling a valvular lesion (Gleason, 1955). On the other hand a major embolic catastrophe may occur as in the case described above or the whole tumour may even become dislodged (Brewin, 1951).

The case under discussion showed the following unexplained features at the time of assessment:—

1. The case was apparently one of peripheral embolus but no source for the embolus was demonstrable.

2. There was no history to suggest peripheral vascular disease.

3. There was some indefinite history of cardiac disease but no evidence of valvular disease or auricular fibrillation.

4. At operation the embolus was of a most unusual appearance.

In retrospect, appreciation of the importance of these facts might have led to clinical awareness of the true state of affairs.

SUMMARY

A case of myxoma of the left atrium with peripheral emboli is described. It is considered to be more than a curiosity in that peripheral embolus may be the manner of presentation of such a tumour. Since the primary condition may occur in the young and may nowadays be amenable to treatment, it is worth bearing the tumour in mind in a case of peripheral embolism presenting unusual or unexplained features.

We would like to express our thanks to Mr. F. R. R. Martin for permission to publish details of the case, and to Mr. J. Hainsworth for the photographs.

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ANEURYSM OF THE MAIN PULMONARY ARTERY

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ANEURYSM of the main pulmonary artery is rare. No mention of it is made in a symposium on aneurysms in the proceedings of the International Society of Surgery for 1953. In view of the uncommon site, the following case is reported.

CASE REPORT

The patient, a well-nourished, healthy-looking woman of 41 years, had noted breathlessness on exertion since a pregnancy seventeen years before. At that time valvular disease of the heart had been diagnosed. In the ensuing years there had been little change until recently, when slight deterioration had been noted. Thus when first seen in 1957, she could walk 100 yards at a slow pace on the level or she could climb slowly one flight of stairs before becoming breathless. Paroxysmal non-productive coughing had troubled her for years, particularly in the winter months. Occasional swelling of the ankles towards the end of the day was the only other symptom she had noticed.

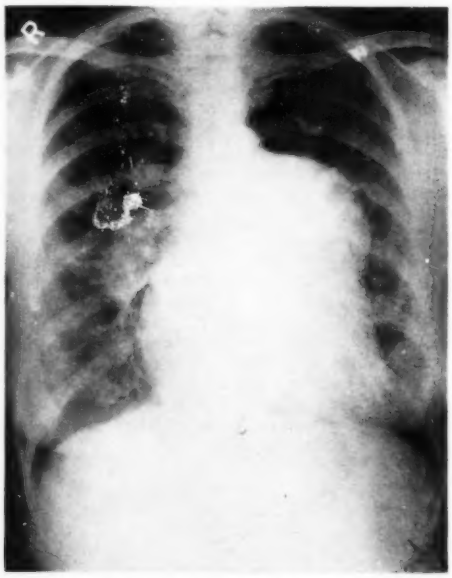

FIG. 405.—Two-metre chest film to show the aneurysm shadow bulging on the left upper salient of the heart outline.

She had had the usual childhood illnesses; apart from these her health had been good. The only relevant family history was that a niece had been born with "abnormal heart valves".

On examination there was a moderate malar flush. The pulse was regular in time and force, 70/min., B.P. 120/85 mm. Hg. The precordium appeared normal; the area of cardiac dullness was increased to the left. The apex beat was right ventricular in character and it was easily palpable in the 5th left intercostal space, 4½ in. from the mid-sternal line. A faint thrill during ventricular systole could be felt over the base of the heart and was most marked over the inner ends of the left 2nd and 3rd intercostal spaces. Auscultation over this same area confirmed a ventricular systolic murmur, maximal at the base and fading towards the apex. At this latter site there was also audible a crescendo auricular systolic and a ventricular diastolic murmur.

Electrocardiographic examination indicated right axis deviation, abnormal P waves, some myocardial changes, and occasional auricular extrasystoles. Fluoroscopy and radiography showed enlargement of the heart, cardio-thoracic ratio = 60 per cent. This appeared to be due to increase in the size of the right ventricle, the left atrium, and the presence of a pulsatile swelling on the left upper border of the heart shadow (*Fig.* 405). This swelling appeared to originate from the main pulmonary artery. The aorta was small.

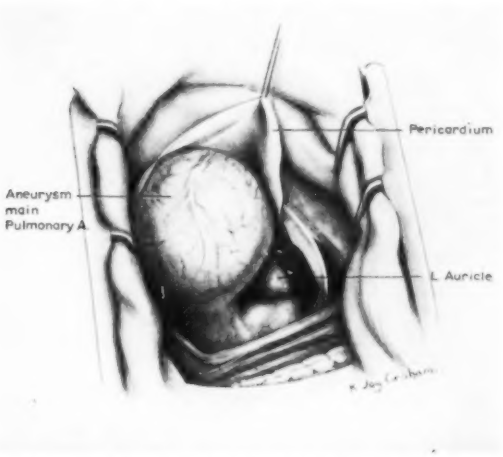

FIG. 406.—Drawing made at the time of operation to show the sac of the aneurysm of the main pulmonary artery.

Cardiac catheterization was carried out. The pulsatile swelling noted on screening was shown to be definitely pulmonary artery main trunk by placement therein of the catheter. The other relevant findings from this examination were: —

Site	*Mean Pressure (cm. saline from mid-thorax)*	*Blood O_2 Content (vol. per cent)*
Superior vena cava	7·5	10·9
Right atrium (mid)	6·5	11·6
Right ventricle	46·0	11·4
Main pulmonary artery	53·0	10·9
Right pulmonary artery	51·0	11·2
Right peripheral pulmonary artery, 'wedge pressure'	28·0	15·4
Left brachial artery	125/85	16·1

From these findings it appeared that there was no obvious intracardiac shunt and from the raised 'wedge pressure' taken in conjunction with the clinical findings the diagnosis appeared to be mitral stenosis and an aneurysm of the main pulmonary artery.

The patient was kept under observation for a further three months, during which the X-ray appearances

remained unchanged but supraventricular extrasystoles appeared more frequently on E.C.G. tracings. The exertional dyspnœa also became worse. Operation, therefore, was carried out.

AT OPERATION.—A left anterolateral thoracotomy was made through the bed of the 5th rib. After opening the tense pericardium, the heart was quite overshadowed by a large aneurysm originating from the root and occupying the whole extent of the main pulmonary artery trunk. The sac was globular, 4 in. in diameter and tense (*Fig.* 406). There was a faint systolic thrill over the pulmonary valve and the aneurysm. The former appeared to be about normal in diameter. The left ventricle was small, as was the aorta. The left auricle was opened and the index finger introduced into a large and clot-free left atrium. The interatrial septum was intact. The mitral valve was the site of a tight stenosis, the ovoid opening being just under 1 cm. in its longer diameter and 0·5 cm. across. There was no incompetence. The medial commissure split with the finger; the lateral had to be cut. The final opening was about 3 cm. in its longer diameter and there was no incompetence. After closure of the auricle the pericardium was stitched tightly around the sac. At this stage it was felt that the pressure in the aneurysmal sac was now less; the wall was thin and felt to be clot-free although, naturally, this point was not investigated too closely.

Apart from the onset of auricular fibrillation on the third post-operative day, which reverted to sinus rhythm after the exhibition of digitalis, the patient had a satisfactory convalescence. She started to work as a waitress seven weeks after operation. Breathlessness does not now occur with normal exercise. X-ray examination indicates that the aneurysmal sac is less prominent, although there is still a faint systolic murmur to be heard over the pulmonary area. The apical murmurs have disappeared.

DISCUSSION

While aneurysm of the main pulmonary artery is rare, dilatation of this vessel and of its branches is common. This latter is met with in cases of increased pulmonary arterial pressure, especially in mitral stenosis. It is also seen in Eisenmenger's complex, interatrial septal defect, Lutembacher's syndrome, and Laubry's syndrome where there has been unequal division of the truncus arteriosus with a large pulmonary artery and a small aorta. It is also seen in some cases of patency of the ductus arteriosus and rarely as an isolated entity, the so-called idiopathic dilatation noted by Oppenheimer (1933).

There will obviously be cases where it becomes rather a nice point when an aneurysm exists and when there is aneurysmal dilatation of the pulmonary artery. This distinction was found to be a difficult one to make at times by Boyd and McGavack during a review of cases in 1939. In the present case, although there was no microscopical examination of the wall, the discrete, globular, and pulsatile swelling occupying the main trunk of the pulmonary artery would seem to merit the description of aneurysm.

In the aetiology of these aneurysms, the usual causes have been cited, namely weakening of the vessel wall and increase of intraluminal pressure. Of the cases previously described, syphilis was thought to be the cause in about one-third, pulmonary atheroma and arteriosclerosis accounted for about another third, while the bulk of the others was thought to be due to some congenital defects of the pulmonary arterial wall. In the present case the Wassermann reaction was negative. A moderate degree of pulmonary hypertension had existed for some time and no doubt there were atheromatous changes in the arterial wall. These had resulted from the mitral stenosis, but were probably not severe. A lung biopsy taken at the time of operation showed changes in the smaller branches of the pulmonary arteries compatible with moderately severe pulmonary hypertension. It seems unlikely, however, that pulmonary hypertension, while undoubtedly a contributing factor, was the chief cause of aneurysm formation. It appears more likely, in the absence of any infection of the pulmonary arterial wall, that there has been some congenital weakness of the vessel wall. This suggestion receives some support from the family history of a niece born with heart disease. A biopsy of the left auricular appendage of the heart taken at operation showed that there were occasional Aschoff bodies. It appears unlikely, however, that the process of rheumatic disease had any weakening effect on the artery wall, although rheumatic arteritis has been described. This patient, in common with many others operated on for mitral stenosis and showing histological evidence of Aschoff bodies in the auricle, had no history of rheumatic fever or any previous streptococcal infection.

As for treatment, little has been reported of this aspect of main pulmonary artery aneurysms. In a case of idiopathic dilatation of the pulmonary artery and its branches in a child, Taussig (1947) reports that Dr. Alfred Blalock wrapped the dilated vessel with cellophane. In the present case the favourable outcome to date would appear to depend on the fact that it has been possible to lower the pulmonary arterial pressure by correction of the mitral stenosis. This, together with the close investment of the sac with pericardium, appears to have arrested the growth of the aneurysm.

I wish to thank Dr. J. D. Olav Kerr and members of his unit for the opportunity to treat this patient. I am indebted to Miss Graham of the Department of Medical Illustration for her drawing made at the operation.

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LYMPHANGIO-ENDOTHELIOMA OF THE ANTERIOR ABDOMINAL WALL

REPORT OF A CASE

By JAMES CALNAN and R. H. COWDELL

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To report a single case in the literature is rarely justifiable unless it is rare or shows some unusual features. The case of a patient seen by us with angio-endothelioma of the abdominal wall appears to meet both of these qualifications and so is recorded here.

CASE REPORT

Mr. G. K., a retired book-packer, aged 66 years, was first seen by one of us in December, 1949, when he presented with a large fungating ulcer of the lower abdominal wall. The diagnosis of angio-endothelioma was not suspected at that time, but the history was interesting and unusual.

In April, 1942, at the age of 59 years, this patient had noticed a lump, the size of a pea, beneath his prepuce; he could feel it but was unable to see it owing to the tightness of his prepuce. Three months later he sought advice from the late Mr. Hugh Whitelocke, who diagnosed a carcinoma of the penis with bilateral involvement of the inguinal nodes. Total amputation of the penis and bilateral orchidectomy was carried out. Healing was uneventful and histologically the specimen showed a squamous carcinoma of the inner aspect of the prepuce, Broder's Grade II.

One week later a bilateral block dissection of the inguinal glands was done, but only one node showed evidence of neoplasm. The other nodes had hyperplastic changes due to inflammation. The wounds were slow to heal, owing to infection, but he was discharged home in

FIG. 407.—The plum-coloured discoloration of the anterior abdominal wall in 1949. There is some radio-dermatitis of the skin of the left groin (arrowed), but none on the abdominal wall.

September, 1942. The Hb was 72 per cent and the W.B.C. 8000 per c.mm., with a normal differential. Some six weeks later radiotherapy to the groins and lower abdominal wall was started, each course lasting for 6 weeks, with an interval of 3 months before the next. X-ray therapy was given on and off for the next 5 years until May, 1947. It has not been possible to discover the dosage given, but it must have been of low intensity for no evidence of radio-necrosis of the skin occurred during that time.

About a year after the groin dissections, the left leg began to swell and in April, 1948, a narrow polythene tube was inserted from just above the left knee to the nipple region in an attempt to relieve the lymphœdema. It failed.

In May, 1946, a hard nodule in the lower anterior abdominal wall was noted, and the X-ray therapy continued. The Hb was then 100 per cent. A year later, in May, 1947, the hard area was about the same, but in November, 1948, this was described as a 'bruised area'.

In December, 1948, some 2½ years since anything suspicious had been noted, a biopsy by Mr. A. S. Till was taken of the skin and subcutaneous tissue of this

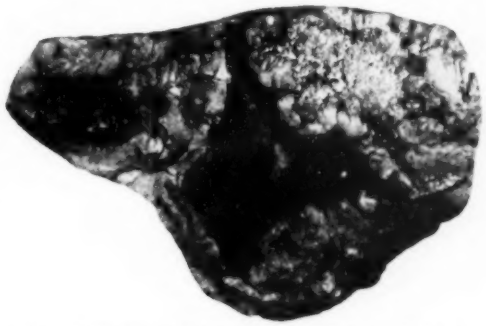

FIG. 408.—Macroscopical appearance of specimen excised in 1950. (× ⅓.)

bruised area: it showed slight capillary and lymphatic dilatation in the dermis with small perivascular aggregates of plasma cells and lymphocytes and no evidence of tumour metastases. The wound healed well, but the area of staining or bruising appeared to increase. By August, 1949, the staining of the abdominal wall was quite large, was much darker and of a plum-red colour, and had a crescentic tender edge below and a crop of fine petechiæ above (*Fig.* 407).

In October, 1949, a further biopsy of the stained skin was taken for it had begun to ulcerate, and was now considered an area of radionecrosis. The histological report noted the infected granulations, active fibroblastic and capillary proliferation with superficial necrosis, and nothing suggestive of malignancy was seen. The Hb had dropped to 80 per cent.

Because the ulcer refused to heal on local dressings a third biopsy was taken in December, 1949. The histological report was similar to the previous ones and the lesion was thought not to be malignant.

Following this biopsy the ulcer rapidly enlarged, showed a necrotic irregular bed, and had a profuse offensive discharge. It was also painful and tender.

In January, 1950, a wide excision by diathermy knife of the anterior abdominal wall down to the rectus fascia was carried out, for it now seemed certain that the ulcer must be malignant (*Fig.* 408). It proved to be an angio-endothelioma of a rather unusual kind.

REPORT ON SPECIMEN.—The specimen (RISH 243/50) consisted of an irregular pentagonal portion of skin and subcutaneous tissue of greatest dimensions 20 × 15 cm. and maximum depth 3·2 cm. There were several areas of ulceration, the largest central ulcer having a depth of 2·5 cm. The base of each was covered by necrotic

hæmorrhagic material through which projected rounded islands of purplish or yellowish firm tissue resembling granulation tissue. The ulcer margins were surrounded by rounded, smooth, œdematous granulomatous masses which overhung the cavity. Some of these masses contained small cystic spaces and channels, in most of which there was no blood. Some of the smaller and more

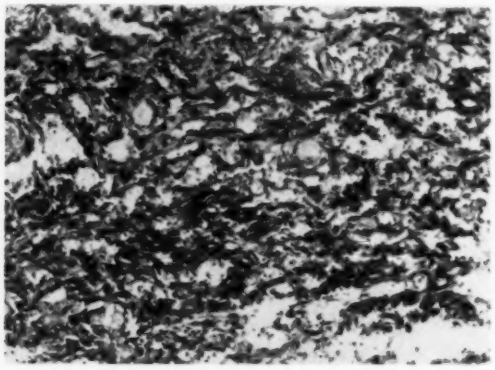

FIG. 409.—Closely arranged vessels with endothelial proliferation and pleomorphism from the deeper part of the tumour. H. and E. (× 80.)

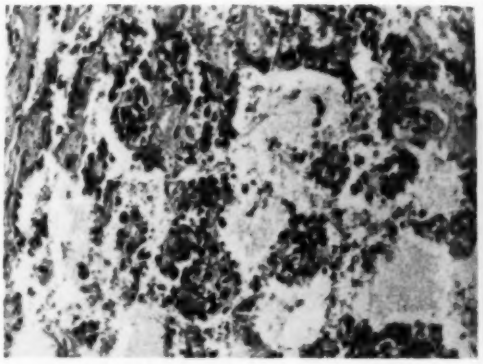

FIG. 410.—Irregular cavernous channels lined by pleomorphic endothelium and separated by hyalinized collagenous tissue. H. and E. (× 80.)

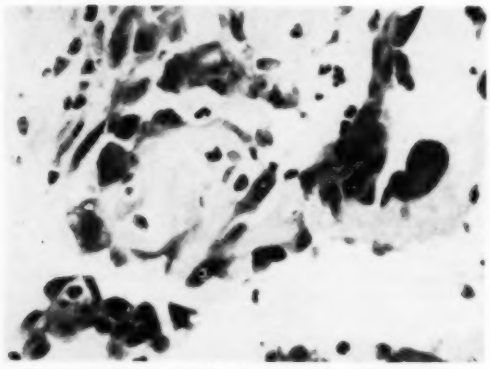

FIG. 411.—Higher magnification of pleomorphic endothelial cells. H. and E. (× 300.)

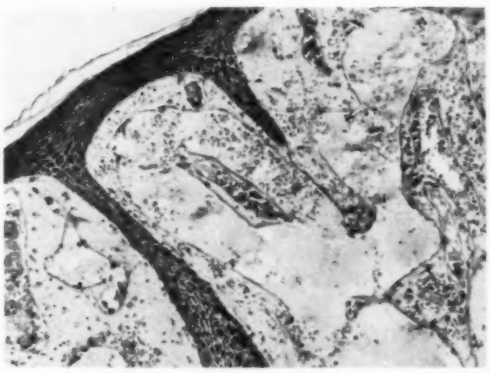

FIG. 412.—Well-differentiated angiomatous area in dermis. H. and E. (× 80.)

superficial ulcers bore crusts. The margin of unaffected skin varied from 1·2 to 2·5 cm. On cutting across the specimen, firm reddish or yellowish tissue of irregular pattern was seen extending into the subcutaneous layers and muscle, and at the base of the largest ulcer it extended to the full depth of resection. The consistence of the tissue varied, some parts being spongy and others firm.

Microscopically, the bases of the ulcers showed a wide necrotic zone beneath which was vascular granulation tissue similar to that seen in the previous biopsy specimens. Deep to this, and in a small area in the centre of the largest ulcer extending right to the lower limit of resection, was œdematous and congested angiomatous tissue. This consisted of irregularly arranged channels and spaces lined by endothelium and separated by fibrous tissue, much of which showed hyaline change. The endothelium showed proliferative activity with a considerable proportion of rounded and pleomorphic cells, and in some places was up to three layers in thickness (*Figs.* 409, 410). Syncytial giant-cell forms and atypical mitoses were both present (*Fig.* 411). In the stroma was diffuse plasma-cell and lymphocytic infiltration.

Most of the channels contained albuminoid deposit. Some were filled with blood, but this chiefly occurred near the necrotic surface where there was polymorphonuclear infiltration and breaking down of the walls, and in other frankly hæmorrhagic areas where there was also hæmorrhage into the stroma. This suggested strongly that the lesion was of lymphangiomatous nature. There was extension in the adventitia of veins around the margin of the affected area, but no involvement of the media or intima. The rounded masses overhanging the ulcer edges were covered by acanthotic and slightly hyperkeratotic squamous epithelium. Beneath this the dermis was œdematous and showed diffuse interstitial hæmorrhage. In the dermis, and extending up very close to the epidermis, were cavernous endothelium-lined spaces, which here even more conspicuously contained only albuminoid deposit with occasional small groups of erythrocytes (*Fig.* 412). The vascular endothelium here was not so obviously proliferative and resembled that of a simple lymphangioma.

In view of the poorly differentiated appearances seen in many areas, the lesion was described as a lymphangio-endothelioma.

SUBSEQUENT TREATMENT.—The raw area was dressed with antiseptic lotions and two weeks later patch grafts

were applied. Most of these failed to take, probably owing to the continued infection of the wound by a mixed growth of organisms. The granulations at the base of the ulcer in places looked darker than usual and an early recurrence was suspected. It was regrafted and was almost healed by March, 1950, but it was now obvious that the tumour had recurred at its original site.

In April, 1950, the whole area was re-excised down to peritoneum and covered by a transposition flap from the

FIG. 413.—Condition after excision of main tumour and repair of anterior abdominal wall. Arrows indicate two small recurrences of the lymphangio-endothelioma.

left thigh which had been 'delayed' some two weeks previously. At this delay operation the opportunity was taken to examine the polythene tube which had been inserted into the leg two years before. It was found to be fractured into short lengths, contained some lymphœdema fluid, and the surrounding tissues appeared to show no reaction.

Catastrophically the distal half of this transposed flap died, necessitating a further flap transposed from the upper abdominal wall.

In June, 1950, all was healed, but two small recurrences were noted and excised. Within a month two further recurrences had to be excised (*Fig.* 413). Two months later a fifth recurrence was excised from near the left iliac crest, and a month later another appeared in the same region.

In January, 1951, the patient became jaundiced and although at the time this was thought to be due to an attack of cholecystitis, it might equally well be related, as a homologous serum hepatitis, to a blood transfusion given three months previously.

Further local recurrences were excised in January and March, 1951. At this stage Dr. Frank Ellis was requested to consider the use of radiotherapy for these multiple recurrences, although we suspected that initially the tumour might be due to the effects of previous irradiation. After nine treatments and a total dose of 2700 r, massive necrosis of the anterior abdominal wall skin occurred.

In December, 1951, he died from secondary deposits in the lungs. Necropsy was refused.

DISCUSSION

From the surgical point of view, the extent of the primary excision of the lymphangio-endothelioma might have been bolder. The lesion could have been excised more widely and more deeply down to peritoneum and the defect covered by transposed skin-flaps from the anterior abdominal and chest wall, and the repair could have been further strengthened by an implant of nylon or terylene in sheet form (Wostenholme, Lotman, and Malament, 1957). But such an undertaking in the presence of gross sepsis and where the diagnosis was still in doubt was hardly justifiable.

When the site of excision was healed and local small recurrences were seen in the repaired abdominal wall, radical surgery was no longer possible nor would it have been accepted by the patient.

The interest in this case from the pathological point of view is in the occurrence of an unusual type of tumour in an unusual situation, and in the relation it may bear to a previous carcinoma, previous radiotherapy, and lymphœdema.

There is a school of pathologists who appear to distrust any tumour reported as a malignant vascular neoplasm. Willis (1948) finds it necessary to ask "Do truly neoplastic angiomatous growths occur?" He admits that they occasionally do, accepting for example the cases of Robinson and Castleman (1936) and Stout (1943), but considers many of the lesions reported as angio-endotheliomata to be hamartomata, and the recorded metastases in these cases to be multifocal hamartomata. In the present case no pathological evidence of metastases can be produced, but the histological picture of the primary growth shows very much more pleomorphism and many more mitoses than are familiar in a simple angioma. It is in the nature of angiomata to have a spreading edge more frequently than a clearly defined encapsulated margin, but the invasion of muscle and venous walls seen here has no counterpart among many simple angiomata studied. The history of the tumour arising in an elderly man and proliferating rapidly both in the first instance and after incomplete excision is also that of a malignant neoplasm, not a hamartoma.

With regard to the evidence that the present lesion is of lymphatic rather than hæmangioid origin, the arguments put forward are identical with those of Stewart and Treves (1948), who in a most interesting paper called attention to the occurrence of tumours which are termed 'lymphangiosarcomata' in lymphœdematous arms following radical mastectomy. Of their 6 patients, 5 had their original operation for carcinoma of the breast, while the sixth was reported as having a benign papillary cystadenoma. In none of them was there any evidence of recurrence of the mammary tumour. Three received pre-operative and 1 post-operative X-ray therapy to the breast or axillary region. The angioid tumours arose between 6 and 24 years after mastectomy and their appearance and behaviour was almost identical with the one here reported. Two of the six have died of pulmonary metastases of the angiosarcoma, and pleural secondaries were suspected in a third. The authors discount radiation as an aetiological factor, since two of the patients had received no radiotherapy and in the remainder the site of origin of the neoplasm did not appear to be within the area of irradiation. They postulate with appropriate reserve the possibility of a systemic carcinogen acting on an area of lowered resistance, the lymphœdematous arm, in an attempt to explain the failure of similar tumours to develop in other diseases involving chronic lymphœdema.

Since the condition was recognized by Stewart and Treves, 13 other cases of lymphangiosarcoma in postmastectomy lymphœdema have been reported

(Nelson and Morfit, 1956) and the additional hazard for those surviving several years after radical mastectomy is becoming more widely recognized. No previous case has been found of a similar vascular tumour following removal of a carcinoma elsewhere, and only 1 arising in an area of lymphœdema not related to mastectomy (Martorell, 1951).

It is necessary to qualify this statement by a brief consideration of Kaposi's sarcoma. McCarthy and Pack (1950) regard the lymphangiosarcomata reported by Stewart and Treves as identical with Kaposi's idiopathic multiple hæmorrhagic sarcoma, and numerous points of similarity in the clinical and pathological findings are obvious. Kaposi's sarcoma usually arises on the extremities and frequently symmetrically. It has a predilection for sites of previous vascular damage, such as varicosities, and œdema so often precedes the appearance of tumours that it has been described as the first event in their development (Bluefarb, 1957). The site of the present lesion on the abdominal wall is rare for Kaposi's sarcoma, but the discoloration similar to bruising is common, as is the histological picture of vascular dilatation and cellular infiltration seen in the first biopsy. In retrospect, there was some vascular proliferation in later biopsies before the large ulcer was excised and the appearances at this stage might have suggested Kaposi's sarcoma although they were far from diagnostic. Bluefarb has collected 10 cases of coexistence of Kaposi's sarcoma with carcinoma, fibrosarcoma, or osteogenic sarcoma, as well as several in association with reticuloses. Kaposi's sarcoma usually appears as multiple dark nodules which are slow to ulcerate, unlike the present lesion, but the most important reason for regarding the tumour now reported as a lymphangio-endothelioma is that histologically it is a vascular tumour without the spindle-cell and fibroblastic proliferation of Kaposi's sarcoma. Accepting that the proportion of vascular and connective-tissue proliferation in Kaposi's tumour may be very variable, one can go to the length of giving a tumour this name when it lacks spindle-cell proliferation entirely (Bluefarb), but the behaviour and histology in this case are entirely those of a vascular tumour. Also, Kaposi's sarcoma is multicentric and may affect almost any organ but does not produce true metastases, which were clinically apparent in our patient and were demonstrated by Stewart and Treves. We are of the opinion that, while the early course of the lesion was consistent with and may have been Kaposi's sarcoma, although with unusual features, in its final stage it was an angio-endothelioma.

While it is generally accepted that radiations of many types may act as carcinogenic agents, and that they may produce vascular changes in the form of endarteritis and telangiectasis, there have been only few reports of vascular tumours arising after and possibly related to the effects of irradiation (Kettle, 1957; Froio and Kirkland, 1952). A classical case was reported by Ross (1932), in which a woman aged 44 years was treated with radium needles for a carcinoma of the breast. One needle became lost in the tissues and was seen radiographically to be lying in the pericardium. It could not be found at operation and was left in situ. The patient died three years later, and among other lesions she was found to have a hæmangio-endothelioma of the liver in a zone immediately subjacent to the needle. The origin of the tumour was traced to the endothelium of branches of the portal vein, and metastases were present in the lungs and bone-marrow. The topographical relationship of the needle to the neoplasm strongly favoured its aetiological relationship. In the present case it is almost certain that the lower abdominal wall received some irradiation during treatment of the inguinal regions, but it is impossible to estimate the dose involved in retrospect.

Martorell's patient was a woman aged 44 years with chronic lymphœdema of both legs. The only significant previous history was that a fracture of the right femur had been plated and on removal of the metal plate there was a wound infection followed by a depressed scar adherent to the bone. Lymphœdema was more severe on this side. Eight months after her first attendance she returned with vegetating nodules in the supramalleolar region of the right leg. These were excised and histological examination revealed lymphangiosarcoma. The first recurrence responded to radiotherapy, but subsequent ones failed to do so and she died shortly after amputation of the leg. No autopsy was performed. This report is of considerable significance in showing that neoplastic change may occur in lymphatics in chronic lymphœdema without previous malignancy or irradiation.

While the aetiological possibilities are interesting, this case also provides an important practical lesson. Vascular neoplasms, like vascular hamartomata, have poorly defined borders, and they require wide excision. Also, a disinclination to regard vascular proliferation as malignant should not be carried to the extent of failure to recognize the rare malignant tumours while they are still operable.

In general, the late results of treatment both by irradiation and radical surgery have been uniformly poor, but Nelson and Morfit (1956) make out a case for plastic surgery. One of their patients treated by extensive excision down to deep fascia and grafting developed no local recurrences. The post-operative course was very satisfactory and although distant metastases developed later, these often follow amputation of an affected limb.

SUMMARY

A case is recorded of lymphangio-endothelioma of the abdominal wall in a patient with lymphœdema which developed after amputation of the penis and block dissection of inguinal lymph-nodes for squamous carcinoma of the penis. The possible factors in the aetiology of the vascular tumour and its relationship to Kaposi's sarcoma are briefly discussed.

Acknowledgements.—We wish to thank Dr. A. H. T. Robb-Smith for giving us his opinion on the relationship of the tumour to Kaposi's sarcoma.

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GRANULOMA OF THE STOMACH

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IN this paper, the term 'granuloma' is employed to describe an inflammatory reaction characterized by the presence of discrete, non-caseating, epithelioid cell tubercles, frequently containing giant cells, and generally surrounded by a zone of lymphocytes. In the case to be described gastric neoplasm was suspected on clinical and radiological evidence, but histological examination of the resected specimen revealed widespread granulomatous lesions of uncertain aetiology and unusual distribution existing as an apparently isolated phenomenon.

CASE REPORT

In November, 1954, the patient, a married female, underwent an exploratory laminectomy on account of symptoms suggestive of a prolapsed intervertebral disk. Apart from vomiting on two occasions in the post-operative period, her convalescence was uneventful and she was discharged on the sixteenth post-operative day.

Three weeks afterwards she developed a constant dull ache localized to the epigastrium and left hypochondrium, the pain being accompanied by the vomiting of food or bile-stained material five or six times daily. These symptoms persisted for three weeks prior to her admission to hospital on Jan. 11, 1955, when she also reported that she had lost 4 st. in weight during the preceding two months. Bowel function had remained undisturbed.

Her previous medical history and that of her family contained no relevant items.

Physical examination revealed no abnormality apart from a laxity of the skin and subcutaneous tissues associated with a recent weight loss. Her blood-pressure was 120/75.

INVESTIGATIONS:—

Barium Meal.—The œsophagus was normal. The capacity of the stomach was much reduced and there was a complete absence of the normal mucosal pattern, only a few distorted rugæ being demonstrated on a limited segment of the greater curvature. The outline of the barium-filled stomach showed a fine irregularity in places, suggestive of superficial ulceration. There was a striking absence of peristalsis, such as was visible consisting of shallow infrequent ripples along the greater curvature. Notwithstanding this almost complete lack of motility, the stomach emptied rapidly, the barium flooding into the duodenum and upper jejunum, both of which appeared normal (*see Fig.* 414). Fluoroscopy and palpation conveyed the impression of marked rigidity of the stomach wall. The radiological diagnosis was considered to be a linitis plastica of neoplastic type.

Gastroscopy.—The reduction of the capacity of the stomach was confirmed. The upper half appeared to be fairly rigid and the mucosa here had a velvety appearance. Instrumentation caused some submucous hæmorrhage at the cardia. Active peristalsis was observed in the pyloric antrum. The appearances were considered suspicious of an infiltrating non-ulcerating carcinoma.

Fractional Gastric Analysis.—Achlorhydria.
Fæces.—Occult blood negative.
Blood.—Hb 74 per cent (11·0 g. per cent).
Urine.—Clear.

AT OPERATION.—At laparotomy, the distal half of the stomach appeared normal but the proximal half was thickened and on its serous surface, which appeared hyperæmic, there were numerous yellowish-white spots.

The changes present did not appear to transgress the cardio-œsophageal junction. The remainder of the abdominal viscera appeared normal.

A total gastrectomy was performed, the œsophagus being anastomosed to a short jejunal loop brought through the mesentery. A secondary side-to-side entero-anastomosis was also performed.

On the thirteenth post-operative day, the patient developed a deep vein thrombosis in the left calf, followed by diarrhœa which remained troublesome for a few days. Culture of the fæces revealed no pathogenic organisms and the condition subsided spontaneously. She was discharged on March 9, 1955.

PATHOLOGY.—Pathological examination of the resected specimen revealed much thickening of the stomach wall (*Fig.* 415) excepting an area in the region of the pylorus. The thickening was due to œdema and fibrosis, which were especially prominent in the submucosa. The mucous surface was congested and superficially ulcerated in a few places and showed six broad, shallow, longitudinal furrows; it had a velvety appearance (*Fig.* 416). The serous surface was as noted at operation. Scattered throughout the whole thickness of the wall there were numerous well-defined granulomatous foci consisting of areas of epithelioid-like cells admixed with small numbers of lymphocytes and giant cells of Langhans type (*Fig.* 417). The lesions showed no necrosis, were discrete, and had a tendency to be arranged perivascularly. The mucous membrane showed plasma cells in increased numbers as well as some neutrophil polymorphs. Acid-fast bacilli were not demonstrated in specially stained sections, nor were organisms seen in Gram or P.A.S. stained sections.

In view of these pathological findings, additional investigations were performed:—

Radiographs of Chest and Hands.—No abnormality.
Wassermann Reaction.—Negative.
Mantoux Reaction.—Positive to 1-1000 old tuberculin.
Serum-proteins.—Total 6·6 g. per cent (Albumin 3·4, Globulin 3·2, A/G ratio 1·09).

FOLLOW-UP.—The patient's condition has remained satisfactory since the time of her discharge from hospital.

On Dec. 13, 1957, further radiographic examination of the small bowel revealed no abnormality, and radiographs of the chest and hands were also normal. Blood-chemistry values were within limits of normal. A macrocytic anæmia with a megaloblastic marrow has developed.

COMMENT

Since a close similarity is observed in the histological features of the pseudotuberculous diseases, the differential diagnosis of the intestinal granulomas on a histological basis frequently poses an insoluble problem. In this group of diseases specific reference must be made to sarcoidosis, since many of the reported cases of isolated gastro-intestinal granulomas have been termed 'sarcoid'. When employing the term 'sarcoid' or 'sarcoidosis', we imply the existence of clinically recognizable systemic disease, preferring the descriptive title of 'sarcoid-like granuloma' for the morphologically similar and apparently isolated lesion encountered in the gastro-intestinal tract and elsewhere. The picture in our case is thus one of 'sarcoid-like granuloma', though the appearances are quite consistent with the presence of sarcoidosis, active tuberculosis, and the non-specific granuloma described by Crohn

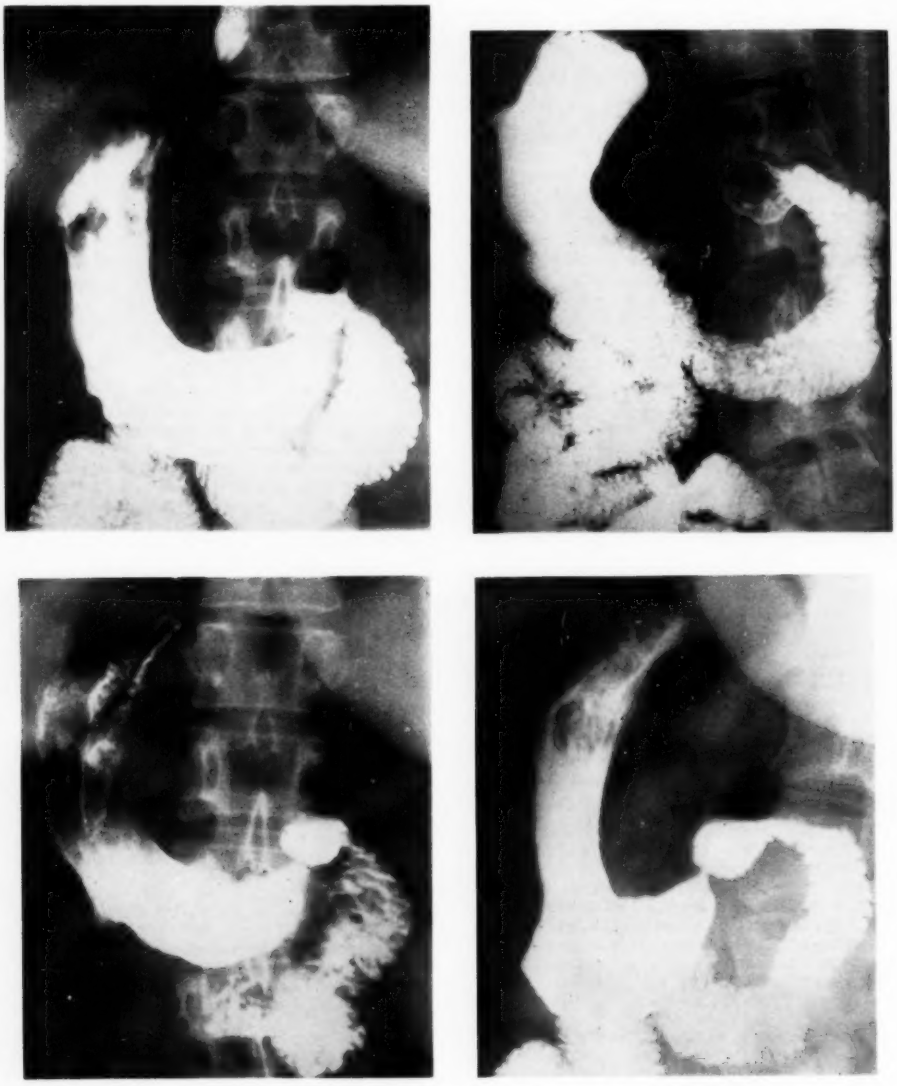

FIG. 414.—The capacity of the stomach is reduced and there is an absence of the normal mucosal pattern. Shallow peristaltic waves are visible on the greater curvature. In places the outline of the barium-filled lumen shows a fine irregularity suggestive of superficial ulceration. The duodenal loop and upper coils of jejunum appear normal.

(1949) and by Comfort, Weber, Baggenstoss, and Kiely (1950).

The existence of apparently sarcoid-like granulomas together with the potential variations in the natural history of sarcoidosis and its relative benignity, renders it difficult to assess the frequency with which this disease involves the gastro-intestinal tract. References in the literature on this point are

FIG. 415.—Transverse section of stomach wall to demonstrate gross thickening of the wall, and loss of normal mucosal folds. (× 2.)

scanty. Longcope and Freiman (1952) investigated 160 cases, including 30 autopsies, and Ricker and Clark (1949) reviewed 300 cases, including 22 autopsies, but in none of these was involvement of the stomach reported. Cowdell (1954) in a series of 90 cases observed only 1 instance in which the gastro-intestinal system was involved, the ileum being affected, but he enumerates many systemic

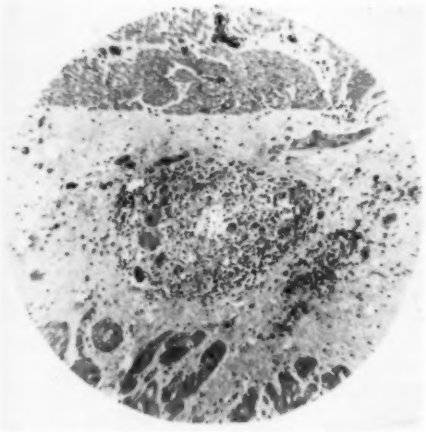

FIG. 417.—Granulomatous focus in the muscle coats of the stomach wall. (× 84.)

diseases in which granulomas resembling those of sarcoidosis have been described. He considered the exclusion of active tuberculosis to be the most difficult problem in differential diagnosis and he emphasized the presence in sarcoidosis of discrete non-caseating epithelioid-cell granulomas showing no evidence of coalescence, containing no tubercle bacilli, and possibly healing by fibrous tissue. Other authors have laid stress on the integrity of the reticulin framework in non-tuberculous lesions. Robb-Smith's (1952) criteria of sarcoidosis consist of typical clinical and histological features, a Mantoux reaction negative to 1–100 old tuberculin and a negative result to a guinea-pig inoculation with biopsy material in six to eight weeks. There is therefore some variation in the diagnostic standards

FIG. 416.—Mucous surface of stomach wall showing its velvety and granular appearance, and loss of the normal mucosal folds. Some of the cracks to be seen are artefacts appearing after fixation of the specimen.

adopted, but in the present case we do not consider that there is adequate evidence for attributing the inflammatory process to sarcoidosis or tuberculosis.

Comfort and others (1950) reported 5 cases where the upper intestinal tract was involved by a granuloma characterized by tubercles identical with those described and regarded as pathognomonic of regional ileitis by Hadfield (1939). In 2 of the cases stomach and duodenum were affected, and in 1 of them, at autopsy, an extension of the inflammatory process to the mesenteric and para-aortic lymph-nodes, and to the peri-adrenal connective tissue was observed. In addition, similar but not identical lesions were noted in the liver. This extension is of interest in view of Hadfield's contentions regarding the relationships of ileitis and sarcoidosis. In his estimation the natural history of sarcoidosis may take many years to unfold and, in view of the paramount importance of the site of involvement in determining the clinical presentation, he considered it unjustifiable to dismiss a possible relationship between ileitis and sarcoidosis until a series of cases of ileitis had been followed for

eight to ten years and no evidence of generalization encountered. Cowdell (1954) followed 9 cases over periods varying from eight to ten years and failed to observe any indication of an extension of the process. Cowdell has also reviewed 15 cases of regional ileitis which demonstrated all stages in the natural history of the disease and found no grounds for assuming a relationship between the two diseases. A similar conclusion was drawn by Watson, Rigler, Wangensteen, and McCartney (1945). The balance of opinion does not favour any relationship between ileitis and sarcoidosis.

Martin and Carr (1953) described 2 cases in which stomach and duodenum were involved by a "chronic granulomatous process like Crohn's disease". In one, involvement of the pyloric antrum, duodenal cap, and proximal half of the second part of the duodenum preceded similar changes in the terminal ileum by three months; in the other, the latter region was initially affected. Allowing for the variations anticipated as a result of the differing disposition of the inflammatory process, the radiological features in the present case bear a close similarity to those described by Martin and Carr, who also indicated the difficulty in differentiating the gastric lesion from neoplasm, and the diagnostic value of duodenal involvement. In addition, they point out that the radiological changes are not necessarily of a permanent nature. In the present report there is no evidence to suggest that the granulomatous reaction represents part of a more widespread disorder.

In most other cases of apparently isolated gastric involvement, the lesions have been pyloric or prepyloric in situation. Bauer (1951) described a granuloma of the pyloric antrum associated with a carcinoma and he made reference to 7 other cases of apparently isolated gastric granulomas described as examples of 'sarcoidosis', several of which were associated with gastric ulceration, the clinical picture resembling a stenosing ulcer or carcinoma. Sherman and Moran (1954 a) described 6 cases, in 3 of which the clinical diagnosis was carcinoma; in 5 of the sites there was associated peptic ulceration. The granuloma in these cases was believed to represent an inflammatory response to the presence of foreign material derived from the access of food particles through ulcerated surfaces, or arising secondarily to the action of the gastric juices on the smooth muscle and fibrous tissue of the gastric wall. They quoted experimental evidence in support of their claim (1954 b). Examination of their illustrations leads us to believe that the lesions are not sarcoid-like granulomas, but are essentially foreign-body reactions. In our case there is no evidence to support a similar identity.

Some difficulty must be admitted in the classification of the apparently isolated granuloma. Crohn (1949) stated it is possible to conceive of sarcoidosis as a localized phenomenon in the intestinal tract, but it is essential to prove convincingly in the interests of diagnostic accuracy that such a lesion is sarcoidosis. In these circumstances, therefore, Bauer's (1951) suggestion of terming these conditions 'sarcoid-like granulomas' appears to us to be sound.

SUMMARY

A case of apparently isolated gastric granuloma of unusual distribution is described. The difficulties in the classification of the isolated lesion are briefly discussed.

Our thanks are due to Mr. A. McKenzie, Consultant Surgeon at Park Hospital, Davyhulme, for permission to publish this case.

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HÆMOPHILIC BLOOD CYSTS

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It is unusual to-day to encounter gross pathological lesions of which no complete account can be found in the literature. Reports of hæmorrhagic cysts or pseudo-tumours in patients with hæmophilia are few in number and inadequate. The nature and origin of these lesions are obscure. Their rarity justifies recording the findings in two patients recently treated, and it is hoped that this account may stimulate further study of the condition.

CASE REPORTS

Case 1.—W. S. (R.I. 169372), a 28-year-old farmer, had suffered from abnormal bleeding since the age of 4 years. Laboratory tests had repeatedly confirmed the diagnosis of hæmophilia and there was a strong family history to support this diagnosis (*Fig.* 418). The main incidents in his history were severe bleeding after tooth extractions, hæmarthrosis of the left hip at the age of 11, a large hæmatoma in the left buttock at the age of 13, and another in the right thigh at the age of 21 in 1949, following mild trauma from walking into a door-handle. At this time he was transfused with blood and was immobilized for five months. The leg was swollen from the toes to the groin. When the swelling subsided a small lump remained in the anterolateral aspect of the thigh muscles. Two years later, in 1951, the mass in the thigh began to enlarge. In April, 1952, 28 oz. of dark brown fluid was aspirated, reducing the lump. A month later, while he was lifting a sack of corn, the mass suddenly enlarged. A second aspiration, after a small transfusion of fresh blood, again reduced the mass.

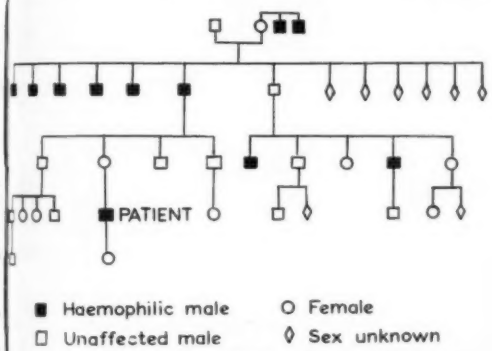

FIG. 418.—*Case* 1. Family tree of the patient.

He was first admitted to the Radcliffe Infirmary under the care of Professor L. J. Witts in January, 1953. On examination the only abnormality was a large fluctuant swelling in the upper two-thirds of the right thigh on the lateral aspect. The skin covering this was normal. The greatest circumference of the right thigh (23¾ in.) was ¼ in. more than the left (19½ in.). An X-ray film showed slight scalloping of the right femur.

On re-admission, in April, 1953, 36 oz. of chocolate-brown fluid were aspirated from the mass and 50 ml. of compatible, fresh, whole blood injected into the cavity and a tight bandage applied. This was removed after six days and he was allowed to stand up to be photographed. The cavity refilled even while the picture was being taken (*Fig.* 420).

He continued at work wearing an extra-heavy elastic stocking to control the swelling, and carried out most of the duties of a farmer. However, in 1955, the swelling increased further and the skin over it began to break down.

He was re-admitted to the Radcliffe Infirmary on July 7, 1955. The maximum circumference of the right

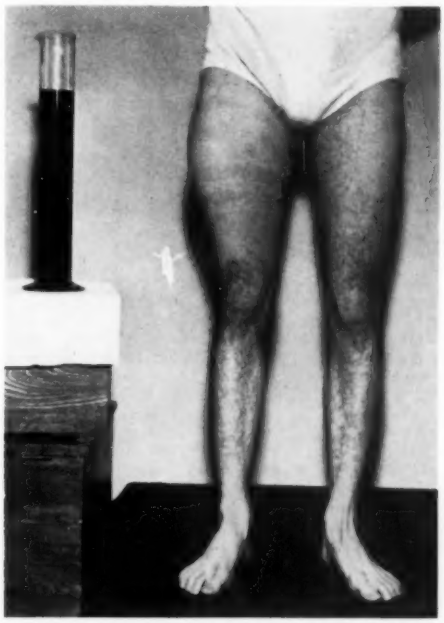

FIG. 419.—*Case* 1. The appearance of the right thigh on April 27, 1953, six days after aspiration of the fluid in the cylinder.

FIG. 420.—*Case* 1. The thigh with ulceration of the skin on July 7, 1955.

* Present address: University of Otago Medical School, Dunedin, New Zealand.

thigh was now 27 in. The skin in this region was tightly stretched, shiny, with large venous channels, and had broken down to leave an ulcer 5 cm. in diameter (*Fig.* 420). Otherwise he appeared to be in good health.

Since the precise nature of the lesion was obscure, further aspiration was done to relieve the strain on the tissues. Fifty-five ounces of dark brown fluid was obtained on July 7. The leg was tightly bandaged and raised, but on July 24 a further 35 oz. was aspirated and there was

FIG. 421.—*Case* 1. Exposure of the deeper cyst.

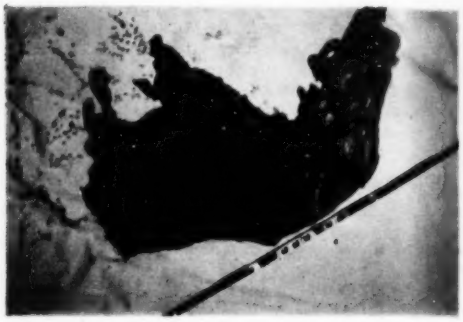

FIG. 422.—*Case* 1. The cyst wall after removal.

no sign of healing of the ulcer, the floor of which consisted of apparently necrotic fascia lata without any signs of tissue reaction. He became febrile and it was feared that the lesion had become infected. It was decided that the time had come for a more radical attack on this swelling. It was hoped that administration of animal anti-hæmophilic globulin (Macfarlane, Biggs, and Bidwell, 1954; Bidwell, 1955 a, b; Fraenkel and Honey, 1955) would correct the coagulation defect sufficiently to make this safe.

At operation on August 2 the ulcer was excised in a long lateral incision. Immediately deep to the fascia lata a cavity containing soft, jelly-like clot was encountered, which extended from the popliteal fossa, where the cyst wall was firmly attached to the shaft of the femur, to the greater trochanter. The wall of the cyst consisted of a tough, fibrous, leathery membrane, about 0·5-1·0 cm. thick, which did not bleed and stripped out easily. It was brownish in colour and shaggy in appearance. Deep and medial to this, in the muscle mass of the thigh, an even larger cavity was found (*Fig.* 421) which contained a different material. Below a thin, chocolate-coloured fluid was a reddish-brown thick granular material of sticky consistency quite unlike any blood degeneration product we had ever seen. The wall was about 1·5 cm. thick, tough and leathery, shaggy inside and of a brownish colour, and of a lighter fibrous colour outside (*Fig.* 422). Again it was stripped out easily except where it was attached to the fibrous septa of the thigh and to the femur. It extended from the inguinal ligament to the lower end of the femur, partly surrounding the femur laterally and behind, and closely related to the femoral vessels in their upper part. *Fig.* 423 shows diagrammatically the situation of the two cysts.

The superficial cyst was excised completely, the deeper one partially, leaving the portions attached to the femur and those closely related to the femoral vessels in the upper thigh, where the precise extent of the cavity could not safely be displayed. The portion related to the knee-joint was also left behind.

During the operation cardiovascular collapse occurred in spite of continuous transfusion of five pints of blood. The cause of this collapse was not obvious. We considered three possibilities: First, that the trauma involved in exploration and evacuation of the cysts was sufficient to produce severe surgical shock. Secondly, that manipulation of the cysts allowed the release of some of their contents into the blood-stream and that these produced the cardiovascular collapse. Finally, it was possible that the animal anti-hæmophilic globulin, which was given during the operation, was responsible. We have little evidence to incriminate any of these factors. The patient recovered well, but developed anuria, of which he died on the eleventh day. Animal anti-hæmophilic globulin was given daily after operation and there was no post-operative bleeding. These aspects of his treatment are not relevant to the present issue, but have been referred to elsewhere (Macfarlane, Mallam, Witts, Bidwell, Biggs, Fraenkel, Honey, and Taylor, 1957).

Two days after operation the patient was slightly icteric and his serum-bilirubin level was 12 mg. per 100 ml. This gradually fell over successive days until on the day before his death it was 5·0 mg. per 100 ml. No pre-operative estimations were done and it is not known whether this hyperbilirubinæmia was due to pre-existing liver damage or anoxia of the liver during operation.

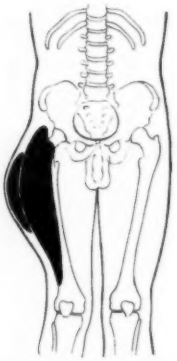

FIG. 423.—*Case* 1. Diagram of the situation of the cysts.

PATHOLOGY (Cyst Wall, R.I.S.H. 4965/55).—The cyst wall consisted of fibrous tissue with old blood-clot adherent to its inner surface. Scattered groups of pigmented macrophages which gave positive staining reactions for iron, and a few lymphocytes and plasma cells were present in the fibrous tissue, but there was no proliferating granulation tissue as might be expected in an organizing hæmatoma. The inner layer of collagen showed hyaline degeneration and focal necrosis. Most of

the blood-clot consisted of granular eosinophilic debris and small irregularly shaped masses of amorphous material which gave a positive benzidine reaction; only scattered groups of red blood-cells of normal shape could be seen.

POST-MORTEM EXAMINATION (R.I.P.M. 562/55).—Beneath the incision in the right thigh was fresh blood-clot which was bounded medially by the femur and elsewhere by gelatinous yellowish thigh muscles.

The liver (2630 g.) was enlarged, yellow, and of soft consistency. The cut surface showed bright-red lobular markings against a yellow background, and in the right lobe there were irregularly shaped grey areas resembling granulation tissue. The appearances suggested a subacute hepatic necrosis. The spleen weighed 580 g. and contained several yellow infarcts. Both kidneys were swollen and œdematous, with a blurred pattern on their cut surfaces. Hæmorrhage had occurred into the bladder and œsophageal mucosæ.

Histological examination of the liver showed a subacute necrosis. The changes varied from a mild centrilobular degeneration to extensive hæmorrhagic necrosis. There was no evidence of an established cirrhosis, but there was some increase in reticulosis with early fibroplastic proliferation.

Sections of the kidneys showed the regenerative phase of an acute tubular necrosis.

Histology of the Thigh Wound.—The blood-clot in the cavity of the wound was of recent formation and in many places contained a well-formed fibrin network. At several points fibroblasts and capillaries were growing into the clot, either directly or through a thin zone of fibrin which lined much of the cavity. In other places there was little evidence of organization and the clot was separated from the adjacent muscle and fibrous tissue by a thin zone of fibrin or by necrotic granulation tissue. Embedded in the granulation tissue was older blood-clot in the form of small clumps of granular material similar to that seen in the surgical specimen of the cyst wall.

A large part of the wall of the cavity consisted of loose œdematous fibrous tissue which merged with the granulation tissue lining parts of the cavity. The fibrous tissue was well supplied with blood-vessels and contained groups of widely separated atrophic skeletal muscle-fibres in its outer parts. The cellular elements in this tissue were mainly large stellate and fusiform fibrobiasts and numerous macrophages. There was also some perivascular infiltration by lymphocytes, plasma cells, and macrophages. The majority of the macrophages and fibroblasts in the inner part of the wall gave a positive staining reaction for iron, and in many of these cells there were obvious hæmosiderin granules. Brown granules were also noted in some of the plasma cells, and some of these gave a positive staining reaction for iron. A wide variety of degenerative changes were present in the muscular tissue. These included atrophy, hyalinization, vacuolization, and loss of normal staining reactions and striations. Many fibres were small and of abnormal shape, their nuclei being central in position. Proliferation of the sarcolemmal nuclei was noted in a few fibres, but regenerative changes were inconspicuous. These changes were regarded as being of a non-specific nature and were presumed to be due to ischæmia caused by the cystic hæmatoma removed at operation, and to abortive attempts at regeneration.

Case 2.—E. G. (R.I. 231743) was a 59-year-old storekeeper. There was no family history of hæmophilia and this diagnosis was not entertained until he was 19 years old. He had played games but suffered from progressive attacks of 'arthritis' so that he had to restrict his activities at the age of 17 and was found unfit for military service.

In 1916 he developed spontaneously a painful swelling in the left buttock and hip with subcutaneous 'bruising'. This was incised and drained. He stayed 16 weeks in hospital before the wound had stopped bleeding and had healed. Two years later he developed a similar swelling in the left groin which was again incised above the inguinal ligament and took 11 weeks to heal. Since then he had had a hæmatemesis, numerous hæmarthroses, a hæmatoma over the left side of the sacrum, and bleeding after tooth extractions. In 1931 his appendix was removed and again he bled for 11 weeks.

In 1950 a swelling appeared in the upper, anterior part of the left thigh, without any preceding trauma. With

FIG. 424.—*Case* 2. The swelling of the thigh.

rest this swelling lessened, but recurred from time to time, and a slowly enlarging mass formed in the left thigh. A similar mass, behaving in the same way, but always smaller, formed in the right thigh between 1950 and 1955.

In August, 1955, a rapid, painful increase of the swelling in the left thigh occurred, attributed to bleeding into it, but aspiration yielded only 30 ml. of blood. He returned to work, but on March 27, 1956, was struck by a bicycle, hurting his left thigh, which swelled to an unprecedented size. He never walked again.

He was admitted to the Royal Hospital, Wolverhampton. The mass continued to increase in spite of repeated transfusions of fresh plasma and fresh blood. He was in constant pain, requiring analgesics, and the lower leg swelled until the skin threatened to break down. On Oct. 1, 1956 he was noticed to be jaundiced and his serum-bilirubin was 7 mg./100 ml. Liver function tests were compatible with a diagnosis of virus hepatitis. He had received 14 pints of blood and 28 pints of plasma. His condition did not improve, and he was transferred to the care of Professor L. J. Witts in the Radcliffe Infirmary on Nov. 1, 1956. He was a heavily built man, jaundiced and with a haggard expression. His protuberant abdomen showed some unfolding of the umbilicus. There was gross limitation of movement of the left shoulder and elbow and both knees. The right hip moved fairly well. The left one could not be tested because of severe pain

in the thigh and lower back. There was a mass in the upper anterior third of the right quadriceps which felt smooth and solid.

The left thigh was enormously enlarged, with shiny skin and prominent superficial veins (*Fig.* 424). A tense, very tender mass extended from the knee to the inguinal ligament, surrounded an adherent deep scar over the greater trochanter, and spread into the buttock to just above the iliac crest. The greatest circumference of the thigh was 29 in. (right 24¼ in.). No fluctuation was found and no bruit heard. Below the mass the left leg was grossly œdematous, pale, and shiny.

A tender mass could just be felt in the left iliac fossa, arising from the pelvis, and there was fullness and dullness of both flanks.

Laboratory tests confirmed the diagnosis of hæmophilia and were compatible with a diagnosis of resolving virus hepatitis. Radiographs of the affected regions gave no additional information, apart from showing scalloping of the shaft of the femur.

Bandaging and elevation of the leg did not reduce the swelling, the viability of the limb was threatened, and the continued pain intolerable. In view of the fatal outcome of *Case* 1, the precise cause of which remains unknown, it was decided to confine the inevitable surgical intervention to a simple turning out of the contents of the swelling if possible.

On Nov. 19, 1956, an incision 11 cm. long was made in the lateral aspect of the thigh. Immediately deep to the fascia lata a huge cavity was entered from which were removed some brownish-red fluid and many handfuls of soft, sticky, putty-like, dark-brown material. The cavity filled the lateral aspect of the thigh from the knee to the hip-joint. Its upper limits could not be defined. The femur was in the medial wall. The cavity was lined with a leathery, tough, shaggy membrane about 2 cm. thick, which did not bleed. It was washed out and drained and a pressure bandage applied as a spica to the whole leg.

On Nov. 22 his temperature rose to 103·6° F. and on Nov. 23 enormous numbers of *Cl. welchii* were identified in the thin fluid oozing from the wound. The wound was immediately re-explored and the cavity found tightly obliterated by great swelling of the surrounding muscles, which were pale yellow, literally running with fluid and so friable that the finger pushed through them easily. Nevertheless the larger vessels bled freely. A diagnosis of *Cl. welchii* myositis seemed inescapable and the cyst wall, with a large amount of the affected muscle, was at once removed, although the part between the hip-joint and the femoral vessels had to be left. The wound was left open. Very large doses of intravenous penicillin were given as well as animal anti-hæmophilic globulin.

HISTOLOGY OF EXCISED TISSUE (R.I.S.H. 8006/56).—The blood-clot on the surface of the muscle consisted of masses of degenerating red blood-cells which were becoming transformed into granular eosinophilic debris. Most of the cells were distorted and fragmented, and there were only very occasional groups of red cells with normal outlines. Fibrin was very scanty and, in many places, only occasional strands could be seen. There were many small solid clumps of faintly granular material of slightly yellowish tint embedded in the blood-clot. Partial encapsulation of large areas of the blood-clot by fibrous septa and by strands of poorly formed granulation tissue had occurred at the deep edge of the clot, but in many

FIG. 425.—*Case* 2. The discharging sinus.

FIG. 426.—*Case* 2. Transverse section of left thigh, showing healing and formation of new cyst.

FIG. 427.—*Case* 2. Diagram of the situation of the cysts.

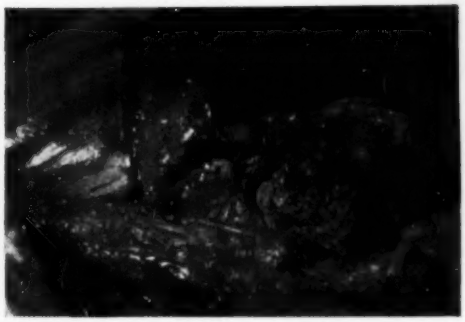

FIG. 428.—*Case* 2. The left-hand cyst perforating the ala of the left ilium seen from the right.

places this connective-tissue framework was necrotic. Micro-organisms were found in the superficial parts; these were Gram-positive cocci and bacilli, the latter having appearances consistent with *Clostridia*.

Deep to the blood-clot was a zone of fibrous tissue containing altered blood, cholesterol clefts, and numerous pigmented macrophages. The macrophages gave a positive staining reaction for iron. More deeply still there

FIG. 429.—*Case* 2. Post-mortem radiograph of right ilium. Some barium in lower cyst.

was a zone of vascular fibrous tissue, and beyond this, muscular tissue.

The muscular tissue showed a marked degree of interstitial œdema with wide separation of the muscle-fibres. The œdema fluid was rich in fibrin, but there was no neutrophil reaction, and only scattered perivascular collections of lymphocytes were present. There was atrophy, interstitial fibrosis, and fatty replacement of the muscle in many places. Individual muscle-fibres were often small and in some instances showed hyalinization and vacuolization. Very occasional necrotic fibres were seen and near the hæmatoma cavity some fibres were completely replaced by fibrin. There were no abnormalities of the blood-vessels, and nowhere in any of the portions of the muscle examined were there any bacteria. Although there was morphological evidence of clostridial infection of the blood-clot lining the wound cavity, the appearances were not those usually associated with clostridial myonecrosis, and although the marked œdema and exudation of fibrin were almost certainly due to the infection, the muscular changes were in keeping with a circulatory disturbance leading to a low-grade ischæmia.

On Nov. 25 the gelatinous watery remains of what were thought to be the hamstrings were excised, and he suffered severe cardiovascular collapse, from which he was restored by rapid intra-arterial blood transfusion.

It would be tedious to relate the innumerable dressings, transfusions, and under-stitchings of points of secondary hæmorrhage which punctuated his further course. The *Cl. welchii* infection was controlled and a mixture of *B. pyocyaneus*, *B. coli*, streptococci, staphylococci, etc. replaced it. Nevertheless, the lower part of the wound granulated very well, but a continuous discharge of reddish-brown material (*Fig.* 425) containing very firm,

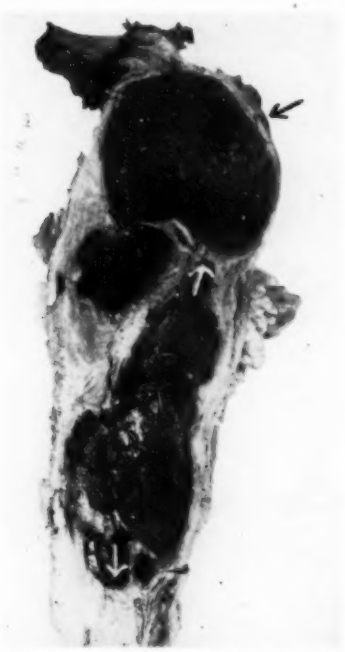

FIG. 430.—*Case* 2. A sagittal section of the right pelvis and upper two-thirds of the right thigh. The black arrow indicates the anterior surface of the iliac hæmatoma; the upper and lower limits of the thigh hæmatoma are shown by white arrows. The posterior extension of the iliac hæmatoma into the gluteal muscles is shown.

ragged concretions up to 2 cm. diameter persisted from the upper part of the wound, where the lesion had not been completely removed. A collection in the buttock was drained on Jan. 9, 1957, when spicules of bare sequestrating bone were felt in the depth of the buttock.

As it was becoming increasingly plain that there was a large reservoir of infection around the pelvic bones which on anatomical grounds could not drain freely, and as the leg was judged pretty useless, a disarticulation through the hip-joint was carried out on Jan. 20, by Mr. R. G. Taylor. The hip-joint was found destroyed, and stinking cavities communicated with the interior of the pelvis. Again, cardiovascular collapse had to be overcome by arterial transfusion. He recovered well, but had a secondary hæmorrhage some days later from the femoral artery, which was arrested. The state of the wound improved somewhat, but his general condition deteriorated and he had some fits which necessitated very heavy sedation. He developed pneumonia and died on Jan. 29 in respiratory arrest.

PATHOLOGY OF AMPUTATED LEG (R.I.S.H. 734/57).—A large V-shaped wound, 25 cm. in length and 12 cm. in maximum breadth, was present on the anterior surface of the thigh. The apex was situated just above the knee-joint; the upper part of the wound narrowed gradually to

become continuous with a groove in the muscle on the upper surface of the specimen. This groove was lined by ragged, brown blood-clot and passed backwards and medially to the undersurface of the neck of the femur. The floor of the wound was covered by light yellowish-brown granulation tissue in which, just above the centre, was a yellowish-grey fibrous tissue of rather gelatinous consistency. Scattered pale-brown areas of muscle, narrow bands of white scar tissue, and mottled yellow areas of fat were visible in this fibrous tissue, but, except for the

FIG. 431.—*Case* 2. A section through the wall of the hæmatoma to show the peculiar character of the blood-clot, and the thick fibrous capsule. H. and E. (× 51.)

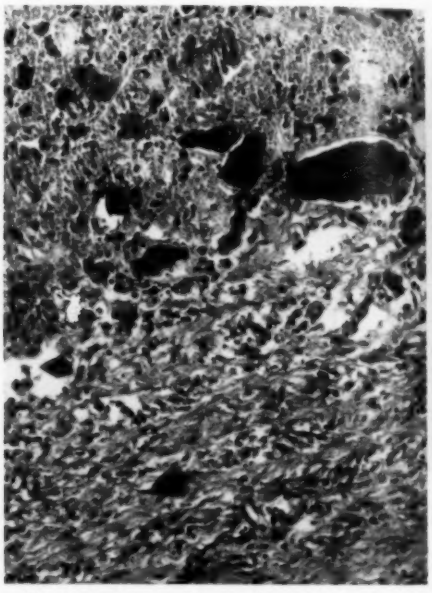

FIG. 432.—*Case* 2. Degenerating blood-clot, granular debris, and solid masses of altered blood at the edge of the hæmatoma. There is little evidence of active organization at the edge of the clot. H. and E. (× 126.)

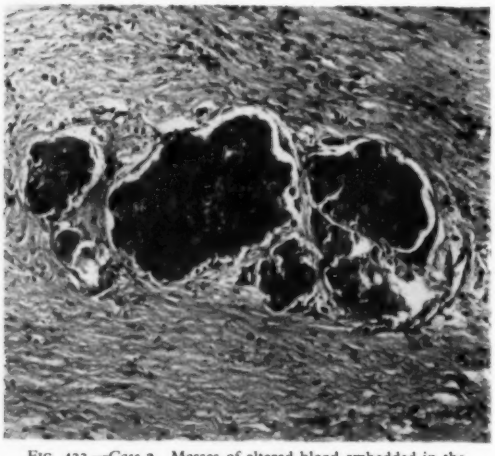

FIG. 433.—*Case* 2. Masses of altered blood embedded in the capsule of a hæmatoma. H. and E. (× 126.)

small sinus. The skin edges were extensively undermined and were bordered by a zone of newly formed epithelium measuring approximately 1·5 cm. in width.

The anterior thigh muscles were greatly distorted and very fibrotic. Most of the tissue between the surface of the wound and the shaft of the femur was translucent sartorius, individual muscles could not be identified. Just beneath the floor of the wound, and communicating with the surface through a small sinus, was a cyst (*Fig.* 426). The cyst measured 7·5 × 3 × 1·5 cm. Another cyst, 5 × 2·5 cm. in main diameters, was present in the fibrotic muscle just lateral to the shaft of the femur. This cyst had a rounded fibrous wall and was full of firm, reddish-brown blood-clot. Beneath the wound edges there were collections of altered blood. Elsewhere in the anterior part of the thigh evidence of old interstitial hæmorrhage was present.

The hamstrings and the muscles of the lower leg showed atrophy and mottled yellow discoloration. A lymph-node near the upper end of the femoral vein showed rusty brown discoloration. Atheroma of moderately severe degree was noted in the popliteal and tibial arteries, but only small flecks of atheroma were found in the femoral artery. The articular cartilage of the head of the femur was brown and pitted. The shaft of the femur beneath the operation wound showed a defect in the cortical bone which appeared to be filled with spongy bone. Old hæmarthroses were present in the knee- and ankle-joints.

POST-MORTEM EXAMINATION (R.I.P.M. 71/57).—The body was that of a middle-aged man with a gaping, infected amputation wound at the level of the left hip-joint. The limbs were wasted but slight fullness of the right thigh was noted.

The main findings were large hæmatomas of the right and left iliacus muscles, a massive hæmatoma of the right thigh, fibrinous pericarditis, and bronchopneumonia. There was a moderately severe degree of atheroma of the coronary arteries, the abdominal aorta, the iliac arteries, and of the right popliteal and posterior tibial arteries. Evidence of old hæmarthrosis was found in all the large

joints examined, and the inguinal, iliac, and para-aortic lymph-nodes showed a rusty brown discoloration.

On each side the iliacus muscle was replaced by a large encysted hæmatoma. Both hæmatomata measured 16 × 13 cm. in main dimensions. On the right side the thigh muscles were largely replaced by a massive cystic

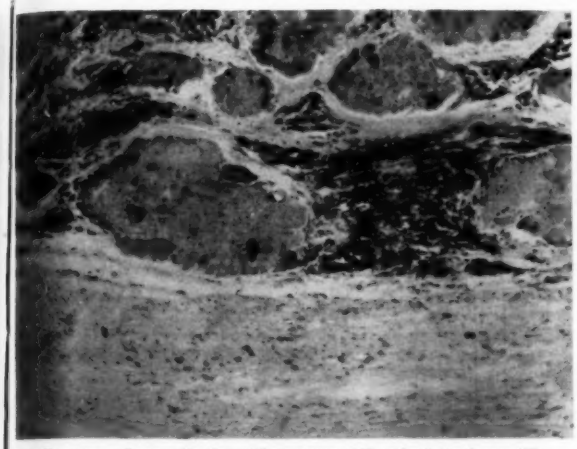

FIG. 434.—*Case* 2. Section of hæmatoma wall stained for iron. The altered blood is surrounded by macrophages which give a strongly positive reaction for iron. (× 126.)

hæmatoma which measured 20 × 19 × 10 cm. These cysts were full of soft, but firmly packed, brown altered blood. In the pelvic cysts there were numerous hard, greenish-black fragments of tissue and some red blood-clot (*Fig.* 427).

The left pelvic hæmatoma (*Fig.* 428) replaced the whole of the iliacus, the lower part of the psoas, the central part of the wing of the ilium, and a large part of the gluteal muscles. Anteriorly and medially the cyst was bounded by a thick fibrous capsule; above, the cyst was bounded by the iliac crest and the muscles attached to it; below, the cyst communicated with the operation wound through ill-defined sinuses which passed beneath the inguinal ligament. The central part of the wing of the ilium presented an oval defect (10 × 8 cm.) through which the hæmatoma extended into the gluteal muscles. The hæmatoma on the right side of the pelvis was almost identical, a similar bony defect in the wing of the ilium, which involved the iliac crest, being found (*Figs.* 429, 430). This hæmatoma extended into the thigh beneath the inguinal ligament, but was separated from the thigh hæmatoma by a fibrous septum.

The hæmatoma in the right thigh (*Fig.* 430) involved all muscle groups and enveloped the upper half of the femoral shaft. The femur was completely surrounded by altered blood, but its periosteum was intact and the bone itself did not appear to be grossly abnormal. The capsule of the hæmatoma consisted of a thick zone of fibrous tissue from which several blunt fibrous septa projected inwards to form ridges on the internal surface. These ridges appeared to be the remains of the intermuscular septa. The surviving thigh muscles were atrophic and largely replaced by fat and fibrous tissue.

Three small encysted hæmatomata were found in the muscles arising from the right iliac crest. All these appeared to be extensions of the iliac hæmatoma. Another small hæmatoma was found in the abdominal muscles just below the ribs; this cyst had no connexion with the pelvic hæmatoma and was not attached to bone.

Histology.—The hæmatomata, both in the amputated leg and in the body post-mortem, all had a similar basic structure. There was a central mass of altered blood-clot which was surrounded by a fibrous capsule (*Fig.* 431).

Much of the blood-clot consisted of masses of closely packed red blood-cells which were undergoing fragmentation and lysis, apparently with eventual transformation into granular debris. Embedded in the clot were solid clumps of altered blood which varied greatly in size and shape (*Fig.* 432). In most of the hæmatomata, but especially in the pelvic hæmatomata, there was some fresh blood-clot in which the red blood-cells were of normal appearance. Fibrin was often present in this fresh blood-clot, but elsewhere was scanty or absent. The degenerating red cells were eosinophilic and stained blue with phosphotungstic acid hæmatoxylin; they gave a positive benzidine reaction, but gave negative staining reactions for iron. Some of the solid masses of altered blood were of yellowish colour and did not give a positive benzidine reaction.

The inner surface of the hæmatoma wall was lined by a thin zone of granulation which merged with the fibrous tissue of the capsule. The granulation tissue was sparse and of poor quality. Capillaries and fibroblasts were less numerous than might be expected at the edge of an organizing hæmatoma and usually did not extend far into the clot (*Fig.* 432). Large masses of altered blood had become incorporated in the fibrous capsule and these were frequently surrounded by macrophages and by multinucleate giant cells of the foreign-body type (*Fig.* 433). Macrophages containing iron pigment (*Fig.* 434) and lipoid were plentiful in the inner layers of the hæmatoma wall. Occasional cholesterol deposits were seen both in the old blood-clot and in the granulation tissue.

The surface of the surgical wound in the amputated leg was covered by a layer of healthy granulation tissue.

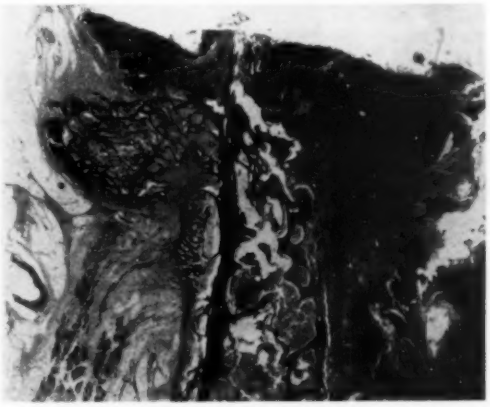

FIG. 435.—*Case* 2. A section taken just below the hole in the right iliac bone. The hæmatoma is eroding the bone anteriorly. Trabecular periosteal new bone is growing into the atrophic gluteal muscles posteriorly. The osteophyte just below the breach in the bone is well shown. H. and E. (× 3.)

Beneath this there was œdematous fibrous tissue which contained groups of atrophic muscle-fibres. The muscle-fibres showed atrophy and degenerative changes similar to those described in the thigh muscle in *Case* 1. In the depths of the wound the cortical bone of a sector of the femoral shaft was replaced by immature trabecular bone, and similar newly formed trabecular bone was growing from the periosteal surface of the bone into the fibrous tissue.

The shaft of the right femur was completely surrounded by altered blood-clot. The bone was not eroded, nor were the appearances suggestive of a subperiosteal hæmatoma. Running through the blood-clot were the remains of the intermuscular septa and the insertions of muscles into the femur.

The pelvic hæmatomata contained much recently formed blood-clot in addition to altered blood. In some situations large capillary blood-vessels were growing into this fresh clot. The fibrous capsules showed hyaline degeneration with areas of necrosis, and the hard fragments of tissue found in these hæmatomata were portions of necrotic, partly calcified, collagen surrounded by altered blood. Destruction of the periosteum and erosion of the inner surface of the wing of the iliac bone had occurred. On the external surface of the wing of the iliac bone there was a zone of newly formed, trabecular periosteal bone (*Fig.* 435) which, at the lower edge of the hole in the ilium, formed an osteophyte. The new bone was growing into the fibrotic gluteal muscles.

The gluteal and thigh muscles showed very marked atrophy, with much fibrosis and fatty replacement. The atrophy was simple in type and was in keeping with a combination of disuse atrophy and ischæmic atrophy.

Microscopical examination of other organs confirmed the macroscopical diagnoses. There was siderosis of the spleen, of the Kupffer cells of the liver, and of the lymph-nodes draining the lower limbs. There was fatty degeneration of the liver, but no evidence of residual hepatitis.

Contents of Cyst from Case 2.— Some of the contents of this cyst were sent to Professor C. Rimington, of University College Hospital. He reported that it consisted of denatured hæmoglobin, some, no doubt, oxidized to methæmoglobin. There was, in addition, a very small quantity of porphyrin and a little free hæmatin present.

DISCUSSION

The management of surgical operations in hæmophilia is discussed elsewhere (Macfarlane and others, 1954; Fraenkel and Honey, 1955; Fraenkel, 1957; Macfarlane and others, 1957). There are many other fascinating problems arising from these cases, but discussion will here be restricted to the nature of the cysts.

A search of the literature has yielded few comparable cases. Only Starker's case (1918) is sufficiently well documented to allow accurate assessment. Erichsen (1856) treated a man aged 34 years with a "hæmorrhagic diathesis" who had "sprained his leg" three years previously, which was followed by swelling of the calf which subsided and recurred. The swelling was needled, infected, and opened, clots being removed. "Some of these clots were rather large and hard, and one of them, about the size of two or three walnuts, was quite decolorized and leather-like in appearance. A cavity was now exposed . . . the walls of which were lined with brown, hardened coagula." Bleeding could not be stopped, amputation was done, and the patient died.

Emile-Weil and Scemama (1936) evacuated a hæmatoma of the hip two months old in a hæmophilic patient who recovered after twenty-five transfusions totalling 12 litres of blood.

Davidson, Epstein, Miller, and Taylor (1949) mention a hæmophiliac of 21 who "developed an apparently spontaneous massive hæmatoma on the left gluteal and thigh muscles with secondary necrosis, slough, and sepsis". Professor Davidson has been so kind as to let us see the original notes of the case. The lesion was 12 days old when the patient was admitted and the skin had already broken down over a gangrenous area posteriorly. His general condition was very poor and he eventually died in spite of energetic treatment. The interesting point is that it appears that pockets of hæmatoma and abscess were distributed throughout the muscles of the thigh and buttock as in our second case, and a feature to us most suggestive is that one year previously he had been admitted with a large, easily palpable mass in the left mid-abdomen and a firm mass in the left flank, with increased resistance in the left kidney region. These are thus interesting points of comparison with our second case. Most unfortunately there was no autopsy.

Kooreman and Hecht (1943) described a 24-year-old hæmophiliac who developed a huge spontaneous hæmatoma in the lateral part of the right thigh at the age of 24 years. It was treated by aspiration for three months, up to 700 ml. of fluid blood being obtained each time. In spite of pressure bandaging it always refilled directly. It became larger and very painful, but Shoemaker advised against operation. After four and a half years the patient returned to Shoemaker, with three perforations over the swelling, 2–3 cm. diameter, discharging infected old blood. He was extremely ill with a hæmoglobin level below 20 per cent. The "old blood masses were removed" (no further detail given) and the wound healed with a puckered scar in seven weeks.

Three years later the patient was seen again with a huge spontaneous hæmatoma above the old scar, which did not absorb in three months. It was incised. "From the enormous hæmatoma cavity, extending from behind the femur to the greater trochanter, came no drop of fresh blood, and about 500 ml. coagula were removed, which . . . in the three-months-old hæmatoma showed no sign of organization." The wound became infected but eventually healed.

Suma and Martin (1954) describe a 32-year-old hæmophiliac who had an acute hæmatoma of the thigh which broke down and became septic. It was incised and emptied and the wound grafted with skin homografts which were later replaced by autografts, with a good take and recovery.

Wright, Doan, Dodd, and Thomas (1948) mention a case of a "large ulcerating lesion on the posterior surface of the right thigh, caused by the sloughing of a spontaneous massive intramuscular hæmorrhage several months before". They give no further detail or result.

A very suggestive case is reported by Parks (1956). A hæmophiliac of 43 was operated on for small-bowel obstruction. "One interesting feature was overlooked (on the X-ray film), namely erosion of the right iliac crest by an old hæmatoma. . . . After he was anæsthetized a mass was felt in the right iliac fossa. . . . This lump proved to be the retroperitoneal hæmatoma previously referred to, the obstructing lesion being in an adjacent coil of bowel." This may well be a case of the type we are describing. Stefanini and Dameshek (1955) show an X-ray picture of a large hæmatoma of the left psoas muscle which had caused root symptoms of L.2, 3, and 4. They state that this patient later suffered a similar hæmatoma on the right which was diagnosed by another physician as acute appendicitis.

It will be noted that none of these contributions gives much account of the local pathology. Findings similar to ours are described, however, in four papers.

Starker (1918–19) described a 14-year-old boy who had had hæmorrhages all his life since circumcision on the eighth day. There was a family history of bleeding. Eight months before admission a large swelling appeared in the upper right thigh which gradually increased in size. It was now the size of a child's head (circumference 38 cm., left 28 cm.). Radiography showed erosion of the shaft of the femur, with calcification of the elevated periosteum. A diagnosis of sarcoma was made, but aspiration of the lump produced 750 ml. fluid blood, with shrinking of the mass. It refilled in four days. The patient became much weaker and more anæmic and died, having "bled to death into his tumour". Necropsy showed an enormous hæmatoma surrounding the lower two-thirds of the femur, enclosed in stripped-up periosteum and only partially fluid, but largely blackish-red and solid. Detailed histological descriptions are included in this paper of stripped-up periosteum surrounded by a thick fibrous layer, remarkably poor in vessels. Atrophy of the surrounding muscle, with narrowing of the muscle-fibres, was noted. The author postulates that the hæmatoma persisted because of repeated small hæmorrhages into it, which caused a resemblance of the changes to those in a false aneurysm. Finally, Starker emphasizes that as both calcification and bone erosion occur in these hæmatomata they cannot be distinguished from malignant neoplasm on radiological grounds.

Reinecke and Wohlwill (1929) give a detailed description of a hæmophilic patient aged 27 years, who had died of septicæmia from a broken-down hæmarthrosis of the knee. X-ray films of his femur showed scalloping, and dissection displayed a chronic subperiosteal hæmatoma of the shaft of the femur, about 2 cm. deep, with a thick fibrous wall which had ruptured in one place where the hæmatoma extended into the muscles of the thigh. Their illustrations show considerable similarities to our cases. Firor and Woodhall (1936), in an article on 'Hemophilic Pseudotumor', relate that following trauma of the thumb of a 16-year-old hæmophiliac a progressive swelling developed over two years, eventually involving the whole thumb and becoming very painful. Radiography suggested a diagnosis of bone sarcoma because of erosion. The swelling broke down and discharged dark blood. The thumb was amputated and a thick-walled cyst similar to ours found. Although a portion of the wall was left behind, the wound healed in 28 days.

Echternacht (1943), under the title 'Pseudotumor of Bone in Hemophilia', describes a 13-year-old hæmophiliac who sustained a blow on the tibia below the knee. A firm, red, painful lump developed over the course of four months. Radiography again showed bone destruction and, on a diagnosis of sarcoma, radiotherapy was given. Later the hæmatoma, which again had a firm fibrous wall, was evacuated. Severe bleeding followed, disarticulation at the knee was done, but further severe bleeding led to the death of the patient.

In view of the high incidence of interstitial hæmorrhage in hæmophilia, it is surprising that encysted hæmatomata are not reported more frequently. It may be that minor forms do occur but remain undetected because they do not produce severe disability or because symptoms due to them are mistakenly diagnosed or overshadowed by incidents such as a hæmarthrosis. Small cysts might remain undiscovered at autopsy unless a special search were made. One of the remarkable features of interstitial hæmorrhage in hæmophilia is the speed with which it is absorbed. However, it seems likely that in hæmophiliacs, as in normal subjects, hæmatomata which are too large to be absorbed by macrophage activity and organization will be treated as foreign bodies and become encapsulated. The granulation tissue surrounding such hæmatomata may well be more liable to bleed than in normal subjects and, if the blood-clot is deficient in fibrin, organization of the clot is likely to be delayed. Sheering strains, producing changes in pressure in the cavity and further cleavage in fascial planes, may lead to increase in size of the cyst and, by thus reducing pressure, permit further bleeding. Thus a vicious circle might be established, leading to progressive enlargement of the cyst and secondary pressure changes in neighbouring tissues.

Some support for this hypothesis is provided by the histological findings in our cases. Focal necrosis of the granulation tissue and of the fibrous walls of the cysts and a paucity of normal granulation tissue were noted.

An alternative explanation of the original mode of formation of these cysts is that from the beginning they are not ordinary interstitial hæmorrhages but occur in relation to periosteum, bursæ, or fascial planes.

The striking refilling of the cysts after aspiration is in marked contrast to the fact that their walls do not seem to bleed much when exposed at open operation. We have wondered whether the original lesion might have been a small arteriovenous aneurysm, but have found no evidence to support this. The effects of sheering might be invoked to explain their contrasting behaviour.

In the two cases here presented the diagnosis has not proved difficult, but the possibilities of sarcoma and aneurysm must be considered. In July, 1957, a young hæmophiliac was admitted to the Radcliffe Infirmary with a cystic mass in the right calf strongly suggestive of a cystic hæmatoma. This subsequently proved to be a Ewing's sarcoma.

Regarding treatment, we can hardly offer much advice on the basis of two fatal cases. We think that the first patient might not have died if his circulatory collapse had been promptly corrected by arterial transfusion. In the second case, the full extent of the lesion, which precluded any hope of surgical success, could not be established before surgical treatment was begun.

SUMMARY

1. Two cases of chronic cystic hæmatomata in hæmophiliacs are described.

2. The nature and mode of formation of these cysts are discussed in the light of our own observations and of observations of similar cases appearing in the literature.

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DUODENAL MEGABULBUS AND ANNULAR PANCREAS

BY E. E. T. TAYLOR, NORTHAMPTON

DUODENAL megabulbus is an expression used by radiologists to describe an appearance found during barium-meal examination. The clinician is less familiar with the term, as the condition may not in itself give rise to symptoms.

FIG. 436.—A typical appearance of duodenal megabulbus. Mild dyspepsia only. Cause unknown.

Fig. 436 shows the barium-meal radiograph of a boy aged 17 years who had mild dyspepsia and is a typical finding. The duodenal cap is enlarged but not deformed. It empties easily, and there is no clear evidence of obstruction. Treatment was not required.

Four cases are described in which a dilated first part of the duodenum sagged down in front of the second part producing chronic obstruction, 2 of these having an annular pancreas.

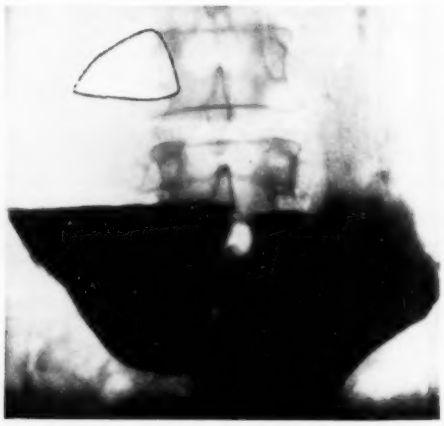

FIG. 437.—*Case* 1. Annular pancreas. Gross enlargement of duodenal cap with fluid level.

CASE REPORTS

Case 1.—**Annular Pancreas.**

A man, aged 54 years, complaining of epigastric and right iliac fossa pain for 7 years. The pain was worse within a few minutes after food, and was apt to wake him at 2 a.m. He had vomited almost daily for one year or more, and had lost 1½ st. in weight.

He was admitted as an emergency to Northampton General Hospital on Sept. 11, 1952, as he had had central abdominal pain for 5 days with repeated projectile vomiting containing bile.

Examination showed a well-built man who had obviously lost weight. His tongue was furred and dry and there was mild tenderness to the right of the epigastrium. Succussion splash present. No visible peristalsis.

FIG. 438.—*Case* 1. After duodenojejunostomy. At 1 hour, showing a working anastomosis.

His condition settled sufficiently for a barium-meal examination to be done on Sept. 19 and this showed (*Fig.* 437):—

1. Gross enlargement of the duodenal bulb with fluid and gas present in it.
2. Widely patent pylorus.
3. Good gastric tone, with normal peristalsis.
4. Evacuation was only possible by laying the patient on his right side in the head-down position.
5. Marked 6-hour delay.

OPERATION (Sept. 26).—Upper right paramedian incision. There was a greatly dilated and thickened first part of the duodenum which was falling over the second part and giving rise to kinking and obstruction at the site of an annular pancreas. The orifice, however, easily admitted a finger. The duodenum distal to the annulus was more bulky than usual. The pylorus was widely patent and the stomach enlarged and thick-walled.

A loop of upper jejunum was brought through the transverse mesocolon and anastomosed to the dilated first part of the duodenum.

There was a tendency to vomit for several days, but thereafter progress was satisfactory.

Subsequent Barium-meal Examination (Dec. 19).—This showed (*Fig.* 438):—

1. Duodenal cap smaller, but still very large, with fluid and gas present.
2. Pylorus not now widely open.
3. Normal peristalsis of stomach and duodenal cap.
4. Anastomosis working well.
5. No delay at 4 hours.

He rapidly regained weight and was completely relieved of all indigestion, gaining 2 st. in weight and returning in every respect to normal health.

On July 24, 1956 he was admitted with small-intestine obstruction by a band. This was released at operation and the anastomosis inspected. This was perfectly healthy. The stomach and duodenal cap were appreciably smaller than when the anastomosis was done. He made an uneventful recovery.

Case 2.—**Duodenal Kink.**

An unmarried woman, aged 40 years, seen as an out-patient on Dec. 7, 1953, complaining of indigestion and dragging pain in the lower abdomen for two months and a feeling of fullness with nausea especially in the morning with vomiting on three occasions.

On examination, a markedly asthenic woman (weight 6 st. 3 lb.) with no definite physical signs.

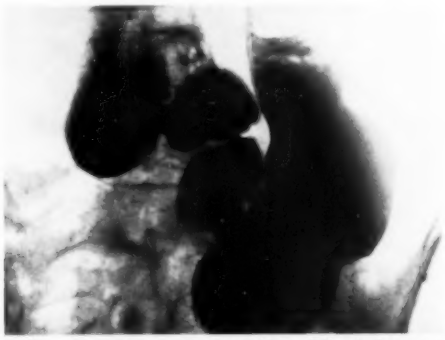

FIG. 439.—*Case* 2. Duodenal kink. Dilated first part of duodenum with hold-up of barium in the cap and in the duodenal loop.

Barium-meal examination had been previously done (Nov. 3, 1953) and showed (*Fig.* 439):—

1. Dilated first part of the duodenum containing gas and fluid and sagging over the second part.
2. Pylorus not widely patent.
3. Normal peristalsis of long stomach.
4. Hold-up of barium at second part of the duodenum in the erect position, apparently due to sagging. The barium passed easily on lying.
5. No delay demonstrated as the patient vomited.

On Feb. 23, 1954 she had been vomiting small amounts every second day for one week. The vomit contained bile. There was some relief of symptoms on lying down.

OPERATION (March 9, 1954).—Upper right rectus split incision. A dilated first part of duodenum was found to be falling over the second part, with consequent kinking and obstruction. It was not thickened. There was no evidence of any distal obstruction.

An upper jejunal loop was brought through the transverse mesocolon and anastomosed to the first part of the duodenum. The appendix was removed.

Convalescence was satisfactory. The vomiting was much relieved, though it still occurred about once a month. She still complained of flatulence. Her weight rose to 6 st. 8 lb. (a gain of 5 lb.), but it was not expected that one of such marked asthenic habitus would ever be completely relieved of symptoms.

On Jan. 11, 1955 she still had a small vomit of food once a week. Her appetite was only fair, and she had to keep to a light diet.

Barium meal was repeated on Feb. 23, 1955 and showed:—

1. Duodenal cap still large, containing gas and fluid.
2. No abnormality of pylorus.
3. Normal peristalsis of stomach.
4. Anastomosis working, but proximal to this barium was still retained longer than in a normal subject.
5. No delay at 2 hours.

Case 3.—**Annular Pancreas.**

A married woman, aged 43 years, seen as an out-patient on April 30, 1955, complaining of indigestion for six years, consisting of fullness after meals with flatulence and

belching relieved by vomiting and improved on lying down. Gradual loss of weight over the past six months. Now vomiting almost daily and unable to eat.

Examination showed a thin woman of medium height. Weight 6 st. 10 lb., talkative and introspective, but bearing up remarkably well under obvious ill health. Visible gastric peristalsis with succussion splash. No abdominal tenderness.

FIG. 440.—*Case* 3. Annular pancreas. Six-hour prone view. Gross enlargement of duodenal bulb. Marked gastric delay.

FIG. 442.—*Case* 3. At operation. Showing marked gastric and duodenal enlargement. The Duval forceps mark the dilated pylorus.

Barium-meal examination had been previously done (April 18, 1955) and showed (*Fig.* 440):—

1. Very large duodenal cap with gross excess of resting fluid and some gas.
2. Widely patent pylorus.
3. Peristalsis present in duodenal cap and long stomach.
4. Hold-up of barium at second part of duodenum which was but little affected by laying the patient down.
5. Marked 6-hour delay.

FIG. 441.—*Case* 3. At operation. The two Duval forceps on the right grasp the duodenum above and below the annular pancreas.

FIG. 443.—*Case* 3. After duodenojejunostomy. Taken when all the barium had been swallowed, showing enlarged cap with fluid level and working anastomosis.

OPERATION (May 25) (*Figs.* 441, 442).—Upper right paramedian incision. Stomach and first part of the duodenum much thickened and dilated. Pylorus widely patent. First part of duodenum observed to contract strongly. Annular pancreas present. This was clearly the site of an obstruction, but the duodenal lumen at this point admitted two fingers and there was no constriction. The obstruction was caused by the first part of the duodenum sagging over the anterior part of the annulus and giving rise to kinking. The small gut below this point was rather larger than normal. Duodenojejunostomy performed.

All symptoms were immediately relieved.

When last seen on Nov. 17, 1955 she was very well. Weight 8 st. 5 lb.—a gain of 1 st. 9 lb.

Barium-meal examination was repeated on July 14, 1955 and showed (*Fig.* 443):—

1. Very large duodenal cap containing fluid and gas.
2. The pylorus was usually closed.
3. The duodenal cap showed good tone.
4. Anastomosis working well.
5. Stomach only contained a trace of barium at 2 hours.

Case 4.—**Duodenal Kink.**

A married woman, aged 40 years, complaining of attacks of vomiting every three months lasting for a week

FIG. 444.—*Case* 4. Duodenal kink. Dilated duodenal cap. Hour-glass stomach due to lesser-curve ulcer.

at a time for the past three years and tending to get worse (Oct. 31, 1957).

She had a feeling of fullness after meals relieved by vomiting, which usually occurred half an hour after food. The quantity was frequently large and consisted of the food taken, followed by bile.

She had no pain but was aware of a 'churning' feeling prior to vomiting. There was no loss of weight. Between the attacks she felt perfectly well.

On examination, a thin but alert and healthy-looking woman. The only abnormality found was a gastric splash.

Barium Meal (Nov. 14).—This showed (*Fig.* 444):—

1. Much enlarged duodenal cap with fluid and gas.
2. Widely patent pylorus.
3. Hypotonic stomach but with normal peristalsis. Hour-glass constriction two-thirds the way up the stomach, associated with a small ulcer.
4. The duodenal cap never emptied properly. The duodenal loop was reversed, being S-shaped. Alteration of position made little difference to the onward passage of barium.
5. Small gastric residue at 3 hours.

OPERATION (Nov. 15).—Upper right paramedian incision. There was an organic hour-glass deformity at the junction of the middle and upper two-thirds of the stomach associated with a small ulcer. The pylorus was widely patent. The duodenal cap was markedly dilated and also thickened. It was clear that kinking occurred just distal to the cap at a place which coincided with the attachment of the pancreas to the duodenum. There was no evidence of annular pancreas and the site was not constricted.

The duodenum distal to this site was more bulky than usual, but there was no evidence of a distal obstruction. The tendency to kink was clearly assisted by laxity of the parts and an undue mobility of the hepatic flexure.

A Polya Hofmeister antecolic partial gastrectomy was performed on account of the hour-glass stomach.

PATHOLOGICAL REPORT.—Benign gastric ulcer. Convalescence was uneventful.

Case 5.—**Cholecysto-gastro-colic Band.**

A man, aged 45 years, seen as an out-patient on Aug. 14, 1958, complaining of increasing vomiting containing bile and food, for 8 months. When he lay on his right side he felt a dragging pain on the right of his abdomen, which was relieved by turning on to his left side.

Barium-meal examination on Sept. 8 showed a large duodenal bulb, but no gastric delay

OPERATION (Sept. 29).—Upper right paramedian incision. The duodenum distal to the dilated bulb was partially obstructed by a cholecysto-gastro-colic band.

Relief was obtained by division of this band followed by duodenojejunal anastomosis.

He was symptomless when seen on Jan. 22, 1959.

A similar case has been recorded by A. Lee McGregor (1936).

DISCUSSION

Duodenal megabulbus is mentioned by Shanks and Kerley (1950) and it is there suggested that it may be due to a congenital defect, to distal obstruction, or be found in hyposthenic patients.

A case is described by Zsebok and Molnar (1952) of a 24-year-old male with epigastric pain half an hour after food, flatulence, and vomiting; on barium-meal examination the presence of a large duodenal bulb with normal second and third parts of the duodenum and no evidence of distal obstruction was suggestive of atony.

The condition is quite distinct from 'chronic duodenal ileus', often known as 'Wilkie's syndrome'.

Finney (1906) described a duodenal dilatation with a widely open pylorus found at operation five years previously. In discussion L. F. Barber suggested duodenojejunostomy as treatment.

J. C. Bloodgood (1907) described 'chronic gastro-mesenteric ileus' and also suggested duodeno-jejunostomy.

Wilkie (1921) described 'chronic duodenal ileus' with five successful instances of duodenojejunostomy. He noted that the duodenal dilatation was usually associated with gastric dilatation and that the pylorus might be widely dilated even to admit three fingers, or may have retained its tone. The condition was usually found in females with visceroptosis.

Wilkie (1927) also recorded 64 instances of duodenojejunostomy for chronic duodenal ileus. Typically, these patients had fullness and flatulence shortly after food, with pain to left or right of the umbilicus half an hour after food and vomiting in bouts lasting one or two days every four or five weeks. The prone or lateral position would afford relief.

Barium-meal examination showed obstruction of the third part of the duodenum.

At operation he almost always found a dilated pylorus and bulging first part of the duodenum. The condition was not always clear even at operation, and where certain evidence was not forthcoming he found that the results of duodenojejunostomy were disappointing.

Telford (1951) refers to the two important X-ray signs of delay in duodenal emptying and dilatation of the duodenum proximal to the site where the mesenteric pedicle crosses it.

The 4 cases now described showed no evidence of obstruction beyond the second part of the duodenum. Comparison of the radiographs makes this difference plain.

In *Case* 1 the first part of the duodenum had fallen down over the second part, producing kinking and obstruction at the site of an annular pancreas. Barium could be made to pass by laying the patient head down on the right side, thus relieving the kink. It was clear from this and from the finding of an absence of actual constriction at operation that the obstruction was caused by kinking of the duodenum across the anterior loop of the annulus.

In *Case* 2 the patient was markedly asthenic and it was understandable that sagging of the stomach and first part of the duodenum could take place.

Here, also, barium passed the obstruction when the patient lay down.

The first part of the duodenum was found dilated, but not thickened, at operation, and kinking due to visceroptosis appeared a satisfactory explanation of the condition.

Case 3 was an obstruction due to annular pancreas and is of interest in that it, too, was caused by kinking of the duodenum over the anterior part of the annulus, and not to compression of the lumen, which admitted two fingers.

Two points are noteworthy: First, an annular pancreas may cause obstruction many years after birth (Silvis, 1952). The fact that in *Case* 1 and *Case* 3 it was caused by kinking and not by compression should account for the delayed onset in these and in other such instances. Secondly, if kinking is the cause of the obstruction this might persist after simple division of the ring. It has been found that this operation may not give relief (Bovill and Bailey, 1952; MacPhee, 1953) and that duodenojejunostomy is preferable (Swynnerton and Tanner, 1953). It is suggested that the mechanism of obstruction in some of the published cases of annular pancreas was the same as in *Case* 1.

Case 4 was of intermittent obstruction due to kinking just distal to the duodenal cap, evidently due again to visceroptosis. As in *Case* 1 and *Case* 3 the duodenum distal to the obstruction also appeared bulky, but this was not due to any distal obstruction.

The gastric ulcer and hour-glass stomach was a further pathological process. H. Daintree Johnson (1955) describes how a gastric ulcer may be formed owing to gastric retention from duodenal ulcer and other causes, and it seems likely that the ulcer was caused in this way.

CONCLUSION

The radiological appearance of 'duodenal megabulbus' (*Fig.* 436) is uncommon. Wilkie (1927) was probably referring to this condition when he stated that: "a dilatation of the duodenum may apparently be present without any detectable mechanical obstruction for reasons as yet unknown". If partial obstruction were the cause one would imagine that eventually surgery would not infrequently be required, but this is evidently rare. Nevertheless, *Case* 2 and *Case* 4 show that partial obstruction can be caused distal to the duodenal cap by kinking, and *Case* 1 and *Case* 3 that annular pancreas can do the same, the obstruction being due to kinking over the anterior band and not to compression of the lumen by the annulus.

SUMMARY

1. An appearance known as 'duodenal megabulbus', occasionally seen on barium-meal examination, is described.

2. Four cases are presented, in each of which obstruction occurred in the second part of the duodenum.

3. A distinction is made between obstruction at the second part of the duodenum and Wilkie's syndrome.

4. The obstructions caused by annular pancreas (*Case* 1 and *Case* 3) were due to angulation over the anterior part of the ring and not to compression of the lumen.

I wish to express gratitude to the late Dr. D. R. Syred who did much work in connexion with this article, and to thank Dr. G. Hollingsworth and Dr. M. C. Connell for help with the radiographs; also Dr. B. Jolles for translation of a reference, Mr. W. Buckley for copying X-ray films, and Mr. E. J. Pamely for the clinical photography.

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GASTRIC CANCER IN YOUNG ADULTS

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"Thirty years of age is a convenient line below which we may consider cancer of the stomach as occurring in the young." Thus wrote Osler and McCrae in 1900 when they reviewed the literature up to that date and described 6 new cases.

Under the age of 30 years gastric carcinoma is rare (Willis, 1948), the majority of cases being found in persons over 40 (Schenken and Burns, 1953; Evans, 1956; Aird, 1957). McNeer (1941) reviewed the recorded cases under the age of 31 and accepted 501, to which he added 5 of his own. Walters, Gray, and Priestley (1942) found only 90 out of 10,890 cases of gastric carcinoma to be under the age of 30. In the survey of cancer in London published by the British Empire Cancer Campaign (Harnett, 1952) there were 1405 cases of gastric cancer, and of these only 3 were in the age-group 15–25 and 24 in the age-group 25–35. Harnett's figures, however, include a few sarcomata.

Sarcoma of the stomach is much less common than carcinoma and is usually stated to constitute about 1 per cent of all malignant gastric neoplasms (Balfour and McCann, 1930; Walters, Gray, and Priestley, 1942; Iason, 1953). Marshall and Meissner (1950), however, reported 41 sarcomata in 1171 operations for malignant disease (3·5 per cent) and Stout (1953) 71 sarcomata in 541 malignant tumours (13 per cent) seen in the laboratory of surgical pathology at Columbia University.

Of the sarcomata found in the stomach, lymphoid tumours are the commonest and leiomyosarcomata next in frequency. Although the average age for sarcoma is less than that for carcinoma the majority of the cases in the published series of lymphoid tumours (e.g., Snoddy, 1952; Skrimshire, 1955; Thorbjarnarson, Beal, and Pearce, 1956) and of leiomyosarcoma (e.g., Chaffin, 1938; Golden and Stout, 1941; Marvix and Walters, 1948; Cowdell, 1950) were over the age of 30.

During the period 1952–56 there were 33 cases of malignant disease of the stomach in British military personnel. Of these 24 were carcinoma and 3 sarcoma; in 6 no histological examination was made. No less than 7 of the cases occurred in soldiers aged 30 or under, and these are described in further detail below.

CASE REPORTS

Case 1.—**Carcinoma.** A male, aged 23 years, was admitted to a hospital overseas in August, 1955, complaining of vomiting after meals for nine months and loss of weight over the previous year.

On examination of the abdomen a small fairly movable lump was found to the left of the umbilicus. Fractional test-meal showed achlorhydria and occult blood was present in the stools. His hæmoglobin was 15·2 g. per cent. Barium-meal examination revealed a large constant-filling defect in the pyloric canal. The patient was transferred to the Queen Alexandra Military Hospital, Millbank, and on Sept. 8, 1955, partial gastrectomy was performed (Lt.-Col. R. A. Stephen).

Pathology.—A large ulcer occupies most of the pyloric antrum and the wall of the stomach in this region is greatly thickened. A number of firm lymph-nodes are present along the lesser curvature.

Sections from the stomach show a carcinoma predominantly of signet-ring cell type. There is extensive infiltration of the muscular coats and the tumour reaches the serosal surface. Eosinophils are numerous, especially in the region of the ulcer. All the lymph-nodes sectioned are invaded by tumour.

Progress.—The patient made a good recovery and by November, 1955, was fit to serve at home in a low medical category. He was readmitted in June, 1956, complaining of vomiting and loss of weight, and died the same month.

At Autopsy.—There was local recurrence at the gastro-enterostomy stoma and extensive carcinomatous involvement of the peritoneum.

Case 2.—**Carcinoma.** A female, aged 23 years, was admitted to a military hospital in May, 1955, complaining of abdominal pain and vomiting for eight weeks.

On examination she was found to be well built with no evidence of wasting. There was an area of tenderness above the umbilicus but no definite mass could be felt. Fractional test-meal showed free HCl to be present. The fæces contained occult blood on one occasion. Her hæmoglobin was 11·5 g. per cent and a stained blood-film suggested mild iron deficiency. Barium-meal examination revealed a persistent filling defect of the antrum.

The patient was transferred to the Queen Alexandra Military Hospital, Millbank, where high partial gastrectomy and splenectomy were performed on June 13, 1955 (Lt.-Col. R. S. Hunt).

Pathology.—On the lesser curvature of the stomach is a large ulcer which extends on to the anterior and posterior walls. There is thickening of the stomach wall in the affected area, especially posteriorly. Several firm lymph-nodes are found along both curvatures. The spleen is normal to the naked eye.

Sections from the stomach show an anaplastic carcinoma. Islets of small darkly staining tumour cells, showing no definite acinar pattern, lie in a considerable fibrous stroma in which are also numbers of lymphocytes, eosinophils, and plasma cells. The tumour extends through the muscle coat to the serosa. All the lymph-nodes sectioned are invaded by tumour.

Progress.—The patient made a good recovery from her operation and was very fit when invalided from the army at the end of July, 1955. Follow-up, however, disclosed that she was again ill in December, 1956, but no further information is available.

Case 3.—**Carcinoma.** A male, aged 30 years, was admitted to a R.A.F. hospital in April, 1956, complaining of loss of appetite and weight for twelve months and of abdominal pain for three months.

On examination of the abdomen an area of tenderness was found to the left of the midline, but no definite mass could be felt. Rectal examination disclosed a hard indurated fixed mass mainly anterior to the rectum. On barium-meal examination the stomach appeared rigid and contracted and no normal peristaltic waves were seen. A diagnosis of carcinoma of the stomach (linitis plastica) was made. At this time his hæmoglobin was 13·6 g. per cent.

Laparotomy was performed (Air Cdre. F. W. P. Dixon) and the diagnosis of carcinoma of the stomach confirmed. Extensive peritoneal involvement was noted and the pelvis was found to be solid with growth. A biopsy was taken from the omentum.

Pathology.—The biopsy shows vascular omental tissue, throughout which are scattered singly and in small

clumps polyhedral tumour cells with irregular hyperchromatic nuclei. The cytoplasm of these cells is strongly P.A.S. positive.

PROGRESS.—The patient was transferred to Queen Alexandra Military Hospital, Millbank, where he died in July, 1956.

AT AUTOPSY.—The peritoneal cavity contained a large volume of blood-stained fluid. The stomach wall was thickened throughout. Giant rugæ were seen in the mucosa, but there was no actual ulceration. Metastases were limited to the peritoneum.

Microscopically there is extensive infiltration of the mucosa and submucosa of the stomach by anaplastic carcinoma. The muscular layers are invaded and tumour cells extend almost to the serosa.

Case 4.—**Carcinoma.** This patient, a 20-year-old male, was admitted to the British Commonwealth General Hospital in Japan in August, 1954, and died in that hospital. Although we have been unable to study any histological preparations, a perusal of the clinical notes and of a well-documented post-mortem report (including histology) leaves us in no doubt that this patient was suffering from carcinoma of the stomach.

Case 5.—**Reticulum-cell Sarcoma.** A male, aged 18 years, was admitted to hospital in August, 1956, complaining of abdominal pain, vomiting, and weakness for one month.

On examination the patient looked unwell, but there was no evidence of weight loss. No superficial lymphadenopathy was found. The liver was palpable and there was a firm mass in the epigastrium. A fractional test-meal showed histamine-fast achlorhydria. His hæmoglobin was 13·3 g. per cent. A barium-meal examination revealed a filling defect at the pyloric end of the stomach.

FIG. 445.—*Case* 5. Reticulum-cell sarcoma. Anterior wall of stomach showing diffuse infiltration by tumour and ulcer in pyloric antrum (A). The muscular layers are still visible (B).

The patient was transferred to the Queen Alexandra Military Hospital, Millbank. Early in September, 1956, partial gastrectomy was performed (Col. A. G. D. Whyte and Lt.-Col. R. S. Hunt). At operation an extensive growth was found in the lower two-thirds of the stomach involving both anterior and posterior walls. The tumour extended higher up the lesser than the great curvature and almost reached the œsophagus.

PATHOLOGY.—The stomach weighs 630 g. There is extensive thickening of the wall by white tissue situated mainly in the submucosa and subserosa, with the muscular coats still clearly visible between these two layers (*Fig.* 445). This thickening involves almost the whole of the lesser curvature and on the greater curvature extends to within 4 cm. of the proximal line of resection. The mucosa overlying the thickened wall is rough and is without rugæ. On the anterior wall 7 cm. from the distal line of resection is an ulcer 2·5 × 2 cm. and 1·5 cm. deep. A number of lymph-nodes are present near the pylorus.

Histologically the stomach wall is infiltrated by a diffuse tumour which does not appear to arise from the gastric glands but it infiltrates between them (*Fig.* 446), and extends outwards through the muscle layers to the serosa. The tumour cells are of uniform size with well-defined nuclei but with little cytoplasm, and do not show any acinar arrangement. A considerable reticulin network is present among the tumour cells. The lymph-nodes show only sinus catarrh.

PROGRESS.—The post-operative course was uneventful and the patient proceeded on sick leave at the end of September, 1956. He died while still on leave in October, but no further details are known.

Case 6.—**Lymphosarcoma.** A male, aged 25 years, was admitted in September, 1955, to a British military hospital in Malaya complaining of vomiting and abdominal pain for two weeks. Fractional test-meal showed free HCl to be present. On several occasions after admission he passed black stools and occult blood was persistently present. His hæmoglobin fell to 5·6 g. per cent at this time. In view of the failure to respond to medical treatment and because of a suspicious barium-meal examination laparotomy was performed on Nov. 20, 1955. An inoperable gastric neoplasm was found. He survived for for a month after his operation, but during this time he had a number of episodes of hæmatemesis and melæna and had to be given further blood transfusions.

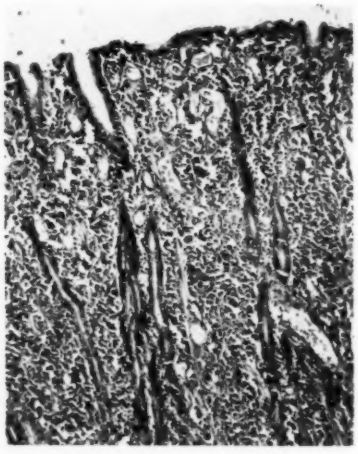

FIG. 446.—*Case* 5. Reticulum-cell sarcoma. Diffuse infiltration of reticulum cells between mucosal glands. H. and E. (× 33.)

AT AUTOPSY.—In the pyloric antrum there was a malignant ulcer 9 × 9 × 4 cm. on the lesser curvature and this had eroded a blood-vessel. Extension of the tumour was restricted to direct spread to the surrounding organs, the diaphragm, and the laparotomy wound, and there was no evidence of generalized disease. The spleen was normal.

Histologically this is a lymphosarcoma composed mainly of large lymphocytes. Mitotic activity is marked. Reticulin is not increased.

Case 7.—**Leiomyosarcoma.** A male, aged 27 years, was fit until the summer of 1954, when he began to suffer from bouts of excessive flatulence lasting up to three days at a time. These attacks became more severe and by October, 1954, he was vomiting food almost immediately after ingestion. His symptoms improved in January, 1955, and he remained fairly well until April, 1956, when he began to vomit undigested food again. At this time he felt that "the food becomes stuck inside my chest". There was no pain and no hæmatemesis. He noted that he had lost weight. In June, 1956, the patient was admitted to a military hospital overseas for investigation.

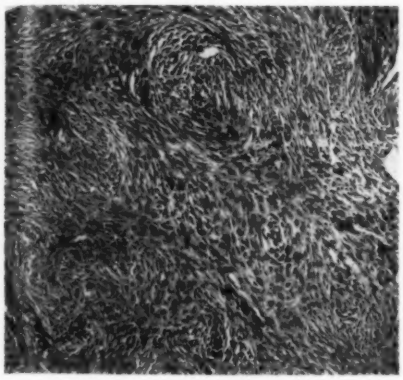

FIG. 447.—*Case* 7. Leiomyosarcoma. Interlacing spindle-shaped cells arranged in whorls and cords. A nest of epithelium-like cells is also shown. H. and E. (× 33.)

On examination the patient was found to be thin and underweight. His hæmoglobin was 14·9 g. per cent. There were no gross physical signs, but a barium-meal examination showed a greatly dilated œsophagus with a stricture at the cardia which did not respond to the administration of amyl nitrite. Œsophagoscopy was performed and the stricture dilated by a bougie. As there was no improvement the patient was transferred to the Queen Alexandra Military Hospital, Millbank, on July 27, 1956.

On Aug. 7 the lower end of the œsophagus and the upper end of the stomach were explored through the thorax (Lt.-Col. R. S. Hunt). The lower 1 in. of the œsophagus and the upper 2 in. of the stomach were found to be hard and irregular. The affected area was resected and the œsophagus anastomosed to the stomach.

PATHOLOGY.—The specimen consists of the lower 3 cm. of œsophagus and upper 7 cm. of stomach. The whole specimen is thickened and the muscle coat of the œsophagus is hypertrophied to a maximum of 0·5 cm. The gastric mucosa is firm, flattened, discoloured, and shows two small ulcer craters 1 cm. and 0·5 cm. in diameter respectively.

A flat, white, ill-defined nodule, 1 cm. in diameter, is present in the subserosa on the posterior aspect of the stomach close to the gastro-œsophageal junction.

Microscopically there is a tumour consisting of interlacing, elongated, and spindle-shaped cells arranged in whorls and cords and of nests of rounded epithelium-like cells (*Fig.* 447). Occasional mitoses are present and much fibrosis is associated with the tumour. Much of the tumour lies external to the muscle coats but it penetrates these at several places, splits up the muscle into cords and bands (*Fig.* 448), and reaches the submucosa. In two places the mucosa overlying the tumour is ulcerated. Elsewhere the muscle coats of the stomach and œsophagus are infiltrated in a diffuse manner and in many areas it is difficult to distinguish tumour from adjacent smooth muscle. A very striking lymphoid hyperplasia is associated with the hypertrophied muscle coats. The white nodule (*see above*) consists of whorls of tumour cells situated in the subserosa.

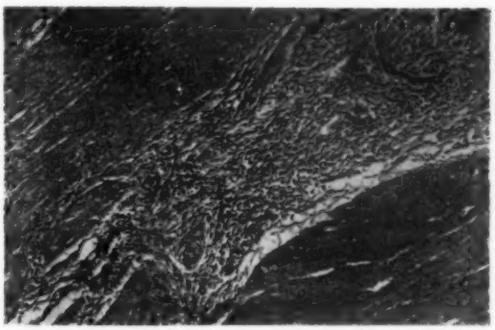

FIG. 448.—*Case* 7. Leiomyosarcoma. Tumour cells penetrating the muscle coats. H. and E. (× 24.)

PROGRESS.—After operation the patient soon began to put on weight. Œsophagoscopy and radiological examination have shown no evidence of recurrence and the patient was fit when last seen (September, 1957).

COMMENT

The population from which our cases were drawn is predominantly one of young adults with only a minority in the age groups in which gastric carcinoma is common. This explains why in five years there were only a small number of cases of gastric carcinoma in the army and why such a high proportion of these were in young adults.

The cases of carcinoma reported above differed in no obvious way from the usual form of the disease as seen in older patients. We agree with McNeer (1941) that age alone should never be allowed to exclude a diagnosis of gastric cancer if everything else points to such a conclusion.

Many have found that it is often not possible to distinguish lymphoid tumours of the stomach from carcinoma on clinical or radiological grounds alone, and that diagnosis depends upon the pathological findings, as in our *Cases* 5 and 6.

On naked-eye examination lymphoid tumours of the stomach are usually either ulcerating, polypoid, or infiltrative (Snoddy, 1952; Skrimshire, 1955). *Case* 5 illustrates well the infiltrative type, whereas in *Case* 6 a large ulcer was the most prominent feature.

Lymphoid tumours of the stomach have their origin in the lymphoid tissue of the mucosa and submucosa. They may be part of a generalized disease or they may arise as primary tumours which spread only locally, at least in the first instance. In *Case* 5 there was no evidence of generalized disease at the time of operation and in *Case* 6 at autopsy the disease was restricted to the stomach and adjacent organs.

Histologically most lymphoid tumours of the stomach are either reticulum-cell sarcomata or lymphosarcomata and a small proportion Hodgkin's

disease. Occasionally the distinction between carcinoma and reticulum-cell sarcoma is not an easy one to make but often, as in *Case* 5, it is obvious that the malignant cells are infiltrating between but not arising from the gastric glands.

Leiomyomata and leiomyosarcomata of the stomach are smooth-muscle tumours arising in the muscular coat and only rarely in the muscularis mucosa (Stout, 1953). Opinions vary on the frequency with which these tumours are found involving the cardia. Some authors (e.g., Watson, 1949; Iason, 1953) have quoted Balfour and McCann (1930) as stating that leiomyosarcoma never occurs in the cardia. Balfour and McCann, however, did not make such a generalization, but only recorded that in their series of gastric sarcomata, which included only 3 tumours classified as myosarcomata, the cardia was never the site of origin. Others (e.g., Chaffin, 1938; Golden and Stout, 1941) found that the cardia was not an infrequent site for smooth-muscle tumours. In our *Case* 7 the tumour arose in the cardia and produced signs and symptoms suggesting achalasia of the cardia. There would appear to be few references in the literature on gastric leiomyosarcoma to cases presenting in such a manner. Pack and McNeer (1935) found that obstruction at the cardia with resulting dilatation of the œsophagus was unusual in sarcoma. However, James (1956) noted that manifestations of obstruction might arise with leiomyosarcomata situated at the orifices of the stomach.

It is often difficult to decide whether a smooth-muscle tumour of the stomach is malignant or not (Golden and Stout, 1941). Both benign and malignant smooth-muscle tumours lack a capsule and the tumour cells may interdigitate with normal tissue at the periphery. If there are many mitotic figures the tumour is probably malignant, although the converse of this is not always true, for in some malignant tumours mitoses have been relatively infrequent (Golden and Stout, 1941). Invasive growth beyond the stomach and hæmorrhages into necrotic areas are considered by Golden and Stout as other indications of malignancy. Taking all these points into consideration we decided to regard the tumour in *Case* 7 as a leiomyosarcoma of low-grade malignancy, for although there are no areas of necrosis and mitotic figures are not frequent there is diffuse infiltration of the stomach and œsophageal wall in the affected area.

If a leiomyosarcoma of the stomach is adequately treated surgically the outlook for the patient is at least fair (Golden and Stout, 1941) and certainly much better than with carcinoma of corresponding extent (Cowdell, 1950). In *Case* 7 the time which has elapsed since the operation is still short and it is obviously too early to think in terms of cure. The fact that the patient is still well and that histologically the tumour is of low malignancy does, however, give encouragement.

SUMMARY

1. Carcinoma of the stomach is rare in young adults. Four cases in military personnel aged 30 years and under are described.

2. One case each of reticulum-cell sarcoma, lymphosarcoma, and leiomyosarcoma of the stomach in young males are also described.

3. The leiomyosarcoma arose in the cardia and gave rise to signs and symptoms suggesting achalasia of the cardia.

Acknowledgements.—We are indebted to the late Professor M. J. Stewart for confirming the diagnosis in *Case* 7; to our surgical colleagues at the Queen Alexandra Military Hospital; to the staff of A.M.D. (Stats) The War Office; to Mr. Tompkinson of the department of photography of the Royal Army Medical College; and to Privates Sirl and Clegg for assistance.

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EXPERIMENTAL SURGERY

ACCELERATION OF WOUND HEALING PRODUCED BY PRELIMINARY WOUNDING

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THE work of Young, Fisher, and Young (1941) and of Sandblom and Muren (1954) suggests that a systemic 'healing state' may be induced in an animal by preliminary wounding and that a fresh wound in such an animal heals more quickly than does the original one.

These findings were not confirmed by Savlov and Dunphy (1954), who found that preliminary wounding elsewhere in the body did not increase the gain in tensile strength in a second wound as compared with a control wound in another animal. However, they did find that wounds which had been disrupted and re-sutured healed more quickly than fresh wounds in other animals. They concluded that the acceleration was due to local rather than systemic factors.

Douglas (1957) investigated the role of the endocrine glands on wound healing and failed to demonstrate any change after the removal of the pituitary, adrenals, or thyroid glands.

It is possible to criticize the above findings on the basis of imperfect control. In the work of Young and others (1941) the healing of the original and new wounds was not synchronous. That is, the original wound was well advanced in healing before the new one was made. In the work of Savlov and Dunphy (1954) a separate series of animals was used as a control. The writer's previous work is open to the same criticism.

Both these sources of error can be overcome if the healing of the original and the fresh wound are studied *simultaneously in the same animal*.

Any systemic effect must then influence both wounds. If under these circumstances the old wound heals more quickly than the fresh wound, the acceleration must be due to local factors in or around the wound. In this paper are presented the results of such a study.

Table I.—SERIES A, 14-DAY WOUNDS

Re-suture Interval	Tensile Strength of Healing Wounds (g.)	
Days	Primary	Secondary
7	678 (4)	956 (4)
14	615 (6)	743 (6)
21	660 (6)	1184 (6)
28	674 (6)	735 (6)
35	747 (4)	873 (4)
42	594 (6)	666 (6)

Figures in brackets indicate number of wounds tested.

METHODS

The test tissue was the lumbodorsal aponeurosis of rabbits, a bilateral structure of fairly uniform tensile strength. The method of testing was by excision of the wounds and the use of a mercury tensiometer (Douglas, 1952). Two initial wounds were made on the right side and sutured. After a varying interval (called the 're-suture interval') the animals were re-anæsthetized, the lumbodorsal fascia re-exposed, the sutures removed, and the wounds re-opened by separation of the blades of a curved hæmostat. Two fresh wounds were then made on the opposite side and finally all four wounds were sutured. The animals were arranged in three series, with six sub-groups in each series; 190 wounds in 48 animals were tested.

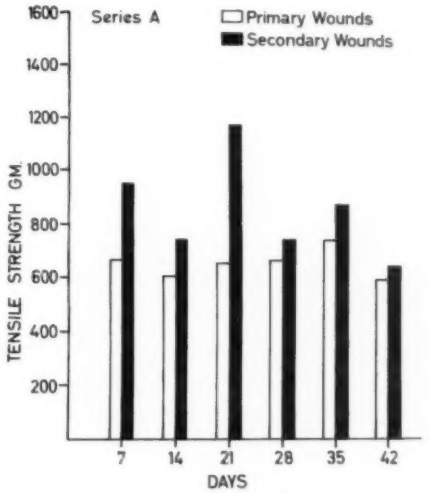

FIG. 449.—Tensile strength of 14-day wounds. When the interval between wounding and secondary suture is 21 days, the secondary wounds are almost twice as strong as the primary wounds.

In Series A the final wounds were tested at 14 days, in Series B at 21 days, and in Series C at 28 days.

The 're-suture intervals' were 7, 14, 21, 28, 35, and 42 days in Sub-groups 1, 2, 3, 4, 5, and 6, respectively.

The sources of error of this method have been discussed previously and are of the order of ±10 per cent.

RESULTS

Series A, 14-day wounds (*Table I, Fig.* 449).—The tensile strength of the secondary sutured wounds was about twice as great as that of the primary wound when the re-suture interval was 21 days. On either side of this period the acceleration effect was still discernible, though at 42 days it had disappeared.

Series B, 21-day wounds (*Table II*, *Fig.* 450).—Similar results were seen in this group. The acceleration effect on the secondary wounds was seen at 7, 14, 21, and 28 days, but was most evident at 21 days.

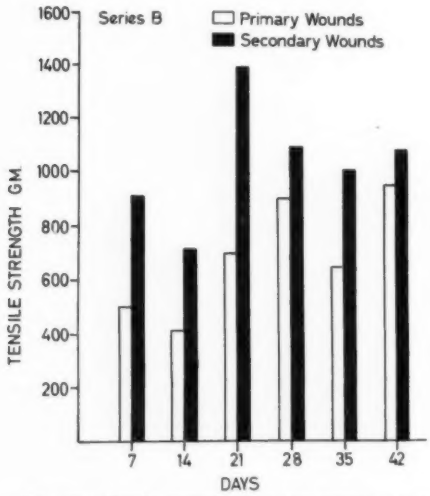

FIG. 450.—Tensile strength of 21-day wounds. As in *Fig.* 449, when the re-suture interval is 21 days the secondary wound is much stronger than the primary.

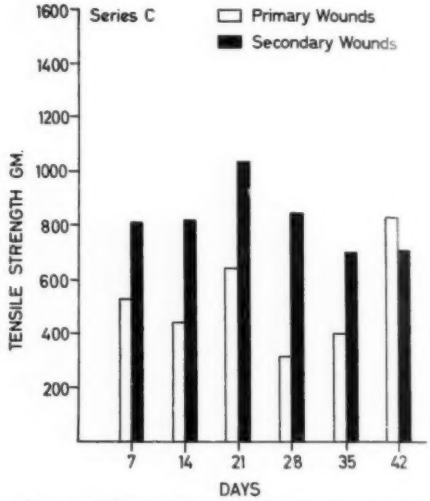

FIG. 451.—Tensile strength of 28-day wounds. Similar findings to those in 14- and 21-day wounds. At 42 days no acceleration effect is detectable.

Series C, 28-day wounds (*Table III*, *Fig.* 451).—In the third series results very similar to the first two were seen, with the maximal effect visible at 21 days.

DISCUSSION

These results indicate that a secondarily sutured wound heals more quickly than a fresh wound in the same animal when both wounds are healing simultaneously.

The hypothesis of a systemic 'healing state' such as was suggested by the work of Young and others (1941) and Sandblom and Muren (1954) hardly seems tenable in respect of these studies, since both wounds would be affected indiscriminately. We must suppose, therefore, that the acceleration is due to local factors in or around the wound, as suggested by Savlov and Dunphy (1954).

What are the possible explanations? The most reasonable view is that the reaction which constitutes the first phase of wound healing has already occurred in the secondary wound. Since the essential elements in this reaction are increased vascularity and fibroplasia, it is likely that the secondary wound would be at a considerable advantage compared with the fresh wound in respect of laying down the connective tissue which gives a wound strength.

In aponeurosis this reaction, judged by the results of these studies, would seem to be at its maximum about 21 days after wounding. This fits in well enough with our knowledge of the slow rate of healing of this avascular tissue. Whereas fibroplasia is at its height in skin wound at about 7 days, it is probably much later in fascia.

What constitutes the local stimulus to fibroplasia in healing wounds?

Davidson reviewed the problem in 1943 and concluded that injured animal tissues produce a factor, or factors, which accelerate tissue proliferation. The nature of this is unknown, though desoxyribonucleic acid, a product of disintegrating nuclei, is known to enhance the growth of tissue cultures. As far as is known it has never been shown to increase the rate of wound healing.

Table II.—SERIES B, 21-DAY WOUNDS

RE-SUTURE INTERVAL	TENSILE STRENGTH OF HEALING WOUNDS (G.)	
Days	Primary	Secondary
7	483 (6)	905 (6)
14	415 (6)	739 (6)
21	703 (4)	1380 (4)
28	915 (6)	1084 (6)
35	650 (6)	1013 (6)
42	959 (4)	1079 (4)

Figures in brackets indicate number of wounds tested.

Table III.—SERIES C, 28-DAY WOUNDS

RE-SUTURE INTERVAL	TENSILE STRENGTH OF HEALING WOUNDS (G.)	
Days	Primary	Secondary
7	533 (6)	803 (6)
14	434 (6)	811 (6)
21	645 (6)	1128 (6)
28	301 (4)	870 (4)
35	380 (4)	751 (4)
42	831 (6)	750 (4)

Figures in brackets indicate number of wounds tested.

SUMMARY

1. Incised wounds were made in the lumbodorsal aponeurosis of the rabbit.

2. After varying periods of time they were exposed, opened, and re-sutured.

3. At the same time fresh incised wounds were made on the opposite side and re-sutured.

4. After an interval, the tensile strength of the re-sutured wounds was tested against that of the fresh wounds.

5. The mean tensile strength of the re-sutured wounds was greater than that of the fresh wounds at all intervals of time.

6. The maximal 'acceleration' effect was seen when the interval between the wounding and re-suture was 21 days.

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INTESTINAL HYPERTROPHY FOLLOWING PARTIAL RESECTION OF THE SMALL BOWEL IN THE RAT

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INTRODUCTION

DURING studies of intestinal absorption in rats subjected to partial resection of the small intestine, we found that enlargement of the distal small bowel frequently followed operations on the upper intestine. At the same time, Loran, Althausen, and Irvine (1956) briefly reported that they had observed generalized dilatation of the small intestine of rats from which as little as one-tenth of the upper small bowel had been removed. It seemed likely that these abnormalities might be of importance in assessing the results of absorption tests in such animals. More detailed studies were therefore carried out to determine the effects of either partial resection or simple division and re-suture on the structure and motility of the small intestine. At varying time intervals after such operations on adult rats, the anatomy and motility of the intestine were studied radiographically following a small barium meal. The animals were killed subsequently and the anatomy of the intestinal tract at autopsy was compared with the radiographic findings. This paper reports the results of these studies.

MATERIALS, METHODS, AND EXPERIMENTAL PROCEDURE

Experimental Animals.—Laboratory-bred male and female hooded rats weighing between 200 and 400 g. were used throughout the experiments.

Experimental Procedure.—Groups of rats were subjected to surgical removal of approximately one-third or two-thirds of the proximal or distal small intestine. In other animals the proximal or distal bowel was divided and then re-sutured, but no resection was carried out. The operations were performed as shown in the table opposite.

It is difficult to measure the length of the small intestine *in vivo*, but approximate measurements may be made when the entire small intestine is stretched out at autopsy (Flint, 1912). In control rats the length of the small intestine ranged from 35 to 40 in. The lengths of the small intestine removed from the rats in which resections were carried out were measured in the same way. Twelve to 14 in. were removed in the case of one-third resections and 22–29 in. when the larger resections were carried out.

Group No.	*No. of Rats*	*Type of Operation*
1	7	Resection of one-third of the proximal small intestine
2	6	Resection of two-thirds of the proximal small intestine
3	6	Resection of one-third of the distal small intestine
4	6	Resection of two-thirds of the distal small intestine
5	6	Division and re-suture at junction of upper and middle thirds of small intestine
6	5	Division and re-suture at junction of middle and lower thirds of small intestine

Six normal rats were used as controls.

Surgical Technique.—The animals were starved for 24 hours before the operations were performed. Under ether anæsthesia the abdomen was opened by a midline incision. When the *proximal* small intestine was resected, the bowel was divided ½–1 in. distal to the duodenojejunal junction, so that the duodenum and approximately 1–2 in. of the proximal jejunum invariably remained. The appropriate length of intestine was then removed. When the *distal* small intestine was removed, the bowel was divided approximately ½ in. proximal to the ileocæcal valve and the appropriate length of intestine was resected proximal to this point. End-to-end anastomosis of the divided ends of the remaining intestine was then performed by means of a single, inverting continuous 5/0 silk atraumatic suture; the gap in the mesentery was repaired. A similar anastomosis was made when the intestine was merely divided and re-sutured. The

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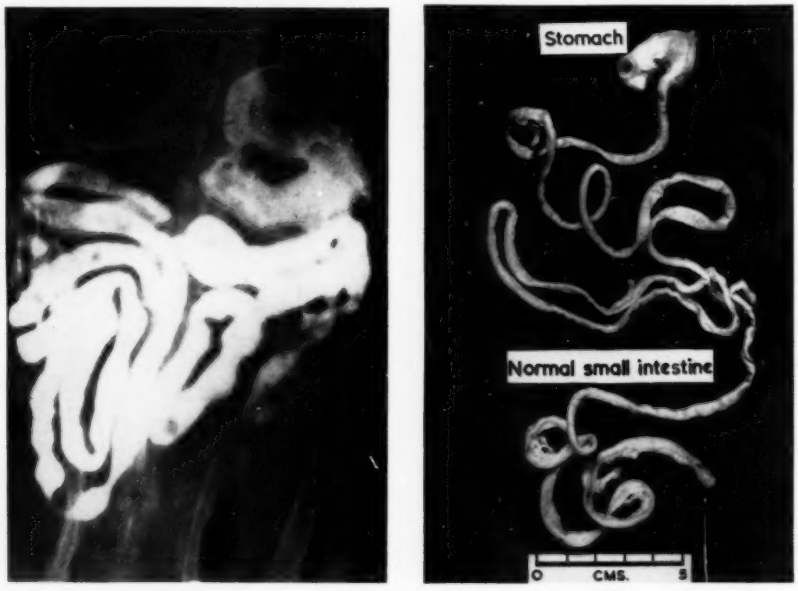
abdomen was closed in two layers, the peritoneum and muscle together being closed with interrupted 2/0 silk sutures and the skin with a continuous 2/0 silk suture. The skin wound was sprayed with 'nobecutane' and no dressing was applied. At the end of the operation the animals received an injection of 10,000 units of crystalline penicillin in 5 ml. of normal saline given subcutaneously. Fluids only were given for 48 hours; thereafter the animals were able to take their normal diet, which consisted of standard laboratory rat cubes.



A B

FIG. 452.—A, Radiographic appearance of small intestine in normal rat. B, Autopsy specimen of small intestine from normal rat.

We confirmed that resection of as much as two-thirds of the small intestine may be well tolerated by rats (Reynell and Spray, 1956), for the animals usually maintained their pre-operative weight. Some animals died in the immediate post-operative phase from peritonitis, obstruction at the site of the anastomosis, or volvulus of the small intestine. Two of the animals subjected to massive distal resection died with diarrhœa and severe marasmus 7–10 days after operation. Only those animals which survived for one month or more after operation have been included in this study. A single rat, in which a distal division and re-suture had been performed, developed a large sacculation at the site of anastomosis and has also been excluded.

Radiographic Technique.—Radiographic studies were carried out at intervals of three weeks to six months after operation. A fine polythene tube was passed into the œsophagus of each animal and 2–3 ml. of a barium suspension (50 per cent micropaque) was injected from a graduated syringe. A 10 in. × 8 in. casette was enclosed in a polythene bag slightly larger than the size of the casette, and was positioned for exposure. The rat was placed in the polythene bag which held the animal in position on the casette. This technique made anæsthesia unnecessary and movement-free radiographs could therefore be taken of fully conscious rats. Radiographs were taken at 36-in. focal-film distance without a grid (Ilford standard screen and films, kV.p. 56; mA. 600; time 0·01 sec.). In rats other than those with large distal resections radiographs were usually taken immediately after feeding the barium and at 30-min. intervals up to 120 or 150 min. In those with large distal resections radiographs were taken at 10-min. intervals. For comparison, similar studies were carried out in the 6 control rats.

The radiographic anatomy of the small intestine was studied and the time taken for the barium to pass from the stomach to the colon was noted. This has been designated the 'intestinal transit time'. Enlargement in the transverse diameter of the small intestine was classified as mild, moderate, or gross.

Post-mortem Studies.—The animals were killed by a blow on the head three to seven months after operation and the anatomy of the small intestine in each rat was compared with the radiographic findings. Histological sections of the small intestine were also examined.

RESULTS

1. Normal Rats.—The radiographic appearance of the small intestine and the post-mortem findings were similar in the 6 control rats. An illustrative radiograph from one animal (Rat 1) is given in *Fig.* 452 A. The post-mortem appearances of the small intestine in this rat are shown in *Fig.* 452 B.

Radiographically, the small intestine in the normal rat was seen to be of uniform calibre and showed a ribbon-like appearance (*Fig.* 452 A); this contrasts with the feathery pattern usually seen in man. The intestinal transit time in the 6 animals ranged from 90 to 165 min. (mean 130 min.). The uniform calibre of normal rat intestine at post-mortem is shown in *Fig.* 452 B.

Table I.—Radiological Appearances and Post-mortem Findings in Rats subjected to Resection of One-third Proximal Small Intestine

Rat No.	Length of Intestine removed (in.)	Radiological Appearances			Post-mortem Findings	
		Time after Operation	Intestinal Transit Time (min.)	Anatomy	Time after Operation	Anatomy
7	12	6 wk.	120	Normal	3 mth.	Slight enlargement in transverse diameter of distal small intestine
8	12	6 wk.	90	Slight enlargement of distal small intestine	3 mth.	Moderate enlargement for 12 in. distal to site of anastomosis
9	12	6 mth.	90	Normal	6 mth.	Normal
10	13	6 mth.	120	Intestine proximal to site of anastomosis normal. Distal intestine moderately enlarged transversely (*Fig.* 453 A)	6 mth.	Intestine proximal to site of anastomosis normal. Distal intestine moderately enlarged transversely (*Fig.* 453 B)
11	14	6 mth.	120	Ditto	6 mth.	Ditto
12	12	6 mth.	90	Ditto	6 mth.	Ditto
13	12	3 mth.	120	Ditto	6 mth.	Ditto
		Mean = 115 min.				

2. Proximal Resections.—The results obtained in the rats from which the proximal small intestine had been resected are given in *Tables I* and *II*. Illustrative radiographs from Rat 10 (one-third proximal resection) and Rat 17 (two-thirds proximal resection) are shown in *Figs.* 453 A, 454 A. The post-mortem specimens from these rats are shown in *Figs.* 453 B, 454 B.

Table II.—Radiological Appearances and Post-mortem Findings in Rats subjected to Resection of Two-thirds Proximal Small Intestine

Rat No.	Length of Intestine removed (in.)	Radiological Appearances			Post-mortem Findings	
		Time after Operation	Intestinal Transit Time (min.)	Anatomy	Time after Operation	Anatomy
14	24	6 wk.	120	Intestine proximal to site of anastomosis normal. Gross enlargement of distal small intestine	5 mth.	Intestine proximal to site of anastomosis normal. Distal intestine grossly enlarged transversely
15	27	6 wk.	120	Ditto	5 mth.	Ditto
16	—	6 wk.	90	Ditto	5 mth.	Ditto
17	—	2 mth.	165	Ditto (*Fig.* 454 A)	5 mth.	Ditto (*Fig.* 454 B)
18	—	2 mth.	165	Ditto	5 mth.	Ditto
19	—	3 mth.	90	Ditto	5 mth.	Ditto
		Mean = 125 min.				

One-third Resection.—Following resection of approximately one-third of the proximal intestine in 7 rats, the intestinal transit time was similar to the control rats, ranging from 90 to 120 min. (mean 115 min.). The intestine was radiographically normal in 2 of these rats studied at six weeks and six months after operation (Nos. 7 and 9, *Table I*). In a single animal (No. 8, *Table I*) there was slight dilatation of the distal small intestine. However, there was moderate enlargement in the transverse diameter of the intestine distal to the site of the anastomosis in the remaining 4 animals (Nos. 10–13) studied at six months after operation (*Fig.* 453). This enlargement was maximal immediately distal to the site of the anastomosis and tapered gradually towards the ileo-cæcal valve. The remnant of proximal small intestine invariably remained of normal calibre (*Fig.* 453 A; *Table I*).

The post-mortem findings confirmed the radiographic observations. In the 5 rats in which the distal intestine was seen to be dilated radiographically (No. 8 and Nos. 10–13, *Table I*) there was moderate enlargement of the distal small intestine at autopsy; the enlargement was most marked immediately distal

to the site of anastomosis and tapered gradually (*Table I; Fig.* 453 B). In the single rat in which the intestine has appeared radiographically normal six weeks after operation, there was slight dilatation distally when the intestine was examined at post-mortem three months later (*Table I*, No. 7). The intestine was found to be normal in only 1 of the 5 rats killed six months after operation (*Table I*, No. 9).

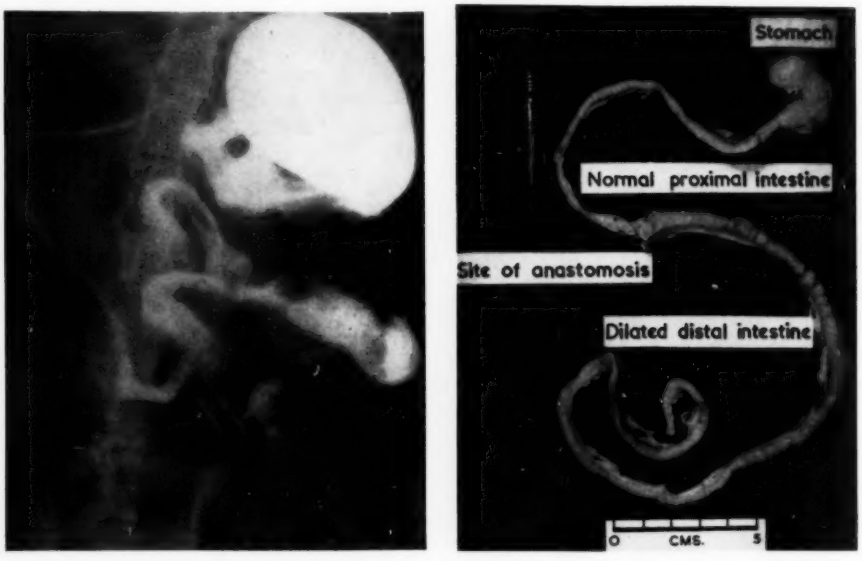


FIG. 453.—A, Radiographic appearance after resection of proximal third of small intestine showing enlargement of the bowel distal to the site of anastomosis (Rat No. 10, *Table I*). B, Autopsy specimen from Rat No. 10.

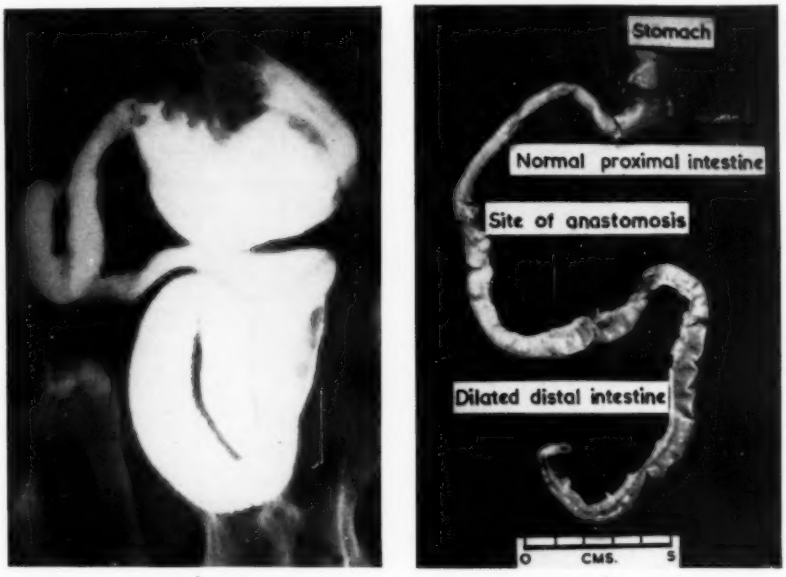
Two-thirds Resection.—Even in the rats in which approximately two-thirds of the proximal small intestine had been resected the intestinal transit time was similar to that in the control rats, and ranged from 90 to 165 min. (mean 125 min.). Radiographically, however, there was gross enlargement in the transverse diameter of the small intestine distal to the site of anastomosis in all these animals (*Table II; Fig.* 454 B); this enlargement was seen as early as six weeks after operation (*Table II*). As in the rats in which one-third resection was performed, the intestine proximal to the site of anastomosis remained normal (*Fig.* 454 B ; *Table II*).

The autopsy findings confirmed the radiographic studies. In all the animals there was gross

Table III.—RADIOLOGICAL APPEARANCES AND POST-MORTEM FINDINGS IN RATS SUBJECTED TO RESECTION OF ONE-THIRD DISTAL SMALL INTESTINE

RAT NO.	LENGTH OF INTESTINE REMOVED (in.)	RADIOLOGICAL APPEARANCES			POST-MORTEM FINDINGS	
		Time after Operation	Intestinal Transit Time (min.)	Anatomy	Time after Operation	Anatomy
20	12	2 mth.	60	Normal	6 mth.	Normal
21	12	2 mth.	60	Normal	6 mth.	Normal. A few adhesions at site of anastomosis
22	12	6 mth.	90	Normal	6 mth.	Normal
23	14	6 mth.	30	Normal	6 mth.	Normal
24	13	6 mth.	60	Slight enlargement of a short segment of the terminal small intestine. Remaining intestine normal	6 mth.	Adhesion at site of anastomosis, intestine enlarged and hypertrophied for 2 in. proximal to this point. Remaining intestine normal
25	12	6 mth.	90	Ditto	—	Ditto
		Mean = 65 min.				

enlargement in the transverse diameter of the distal small intestine; the remnant of proximal intestine was unaffected (*Fig.* 454 B; *Table II*).



A B

FIG 454.—A, Radiographic appearance after resection of proximal two-thirds of small intestine showing gross enlargement of the bowel distal to the site of anastomosis (Rat No. 17, *Table II*). B, Autopsy specimen from Rat No. 17.

3. Distal Resections.—The results in the rats in which comparable amounts of distal small intestine were resected are given in *Tables III* and *IV*.

One-third Resection.—After one-third of the distal small intestine had been resected, the intestinal transit time was more rapid than in the control rats. It ranged from 30 to 90 min. (mean 65 min.). In 4 of the 6 animals the remaining intestine appeared entirely normal, both radiographically and at autopsy (*Table III*). In 2 rats, however (Nos. 24, 25, *Table III*), there was radiographic evidence of localized dilatation of the terminal small intestine, but at autopsy both animals had adhesions at the site of the anastomosis and the intestine was hypertrophied for 1–2 in. proximal to this point; the remaining intestine was normal in calibre (*Table III*).

Two-thirds Resection.—Following resections of two-thirds of the distal small intestine, the intestinal transit time was very rapid and the barium passed into the colon in between 20 and 90 min. (mean 42 min.). In contrast to the results in the rats in which comparable lengths of the *proximal* intestine were resected, radiographic studies revealed no enlargement of the small intestine in four of the six animals (Nos. 26, 27, 30, 31, *Table IV*). In these 4 rats

Table IV.—RADIOLOGICAL APPEARANCES AND POST-MORTEM FINDINGS IN RATS SUBJECTED TO RESECTION OF TWO-THIRDS DISTAL SMALL INTESTINE

Rat No.	Length of Intestine removed (in.)	Radiological Appearances			Post-mortem Findings	
		Time after Operation	Intestinal Transit Time (min.)	Anatomy	Time after Operation	Anatomy
26	22	2 mth.	20	Normal	3 mth.	Normal
27	25	2 mth.	20	Normal	4 mth.	Normal
28	24	2 mth.	60	Slight enlargement of terminal small intestine seen in the film. Remaining intestine normal	6 mth.	Adhesion at site of anastomosis causing partial obstruction, intestine enlarged and hypertrophied for 2 in. above this point. Remaining intestine normal
29	29	2 mth.	30	Ditto	6 mth.	Ditto
30	24	3 mth.	90	Normal	6 mth.	Normal
31	23	4 mth.	30	Normal	6 mth.	Normal
		Mean = 42 min.				

the remaining intestine was entirely normal when the animals were killed three to five months after operation. In 2 animals (Nos. 28, 29) slight enlargement of the distal small intestine was seen in one radiograph. In these 2 animals post-mortem examination revealed adhesions at the site of the anastomosis, with slight enlargement and hypertrophy of the intestine for 1–2 in. proximally.

found to be normal, although there were some adhesions around the site of the anastomosis in 3 (Nos. 32, 34, 37; *Table V*). A single rat (No. 37) showed dilatation of a loop of intestine in one radiograph and at autopsy there was enlargement and hypertrophy of the bowel for 2 in. proximal to the anastomosis, which was partially obstructed by adhesions.

Table V.—Radiological Appearances and Post-mortem Findings in Rats subjected to Division and Re-suture of the Small Intestine Proximally

Rat No.	Site of Division and Re-suture	Radiological Appearances			Post-mortem Findings	
		Time after Operation	Intestinal Transit Time (min.)	Anatomy	Time after Operation	Anatomy
32	Junction of upper and middle third of small intestine	2 mth.	120	Normal	6 mth.	Normal. A few adhesions at site of anastomosis
33	Ditto	2 mth.	90	Normal	6 mth.	Normal
34	Ditto	2 mth.	120	Normal	7 mth.	Normal. Some adhesions at site of anastomosis
35	Ditto	2 mth.	90	Normal	7 mth.	Normal
36	Ditto	2 mth.	120	Normal	7 mth.	Normal
37	Ditto	3 mth.	120	Slight enlargement of a loop of intestine seen in one film	6 mth.	Adhesions at site of anastomosis causing partial obstruction. Intestine slightly enlarged for 2 in. proximal to this point. Distal intestine normal
		Mean = 110 min.				

4. Simple Division and Re-suture of Small Intestine.—The results in the rats in which the small intestine was simply divided and re-sutured are given in *Tables V* and *VI*.

Upper Intestine.—Division and re-suture at the junction of the upper and middle thirds of the small intestine had no effect on the distal bowel. The intestinal transit time ranged from 90 to 120 min. (mean 110 min.) in these rats. Radiographic studies two to three months after operation showed that the intestine was normal in 5 of the 6 animals, and at autopsy the calibre of the intestine in these rats was

Distal Intestine.—Similar studies in the rats whose intestine had been divided and re-sutured at the junction of the middle and lower thirds of the small intestine showed that this operation produced no significant changes in the intestinal transit time or calibre of the bowel. The intestinal transit time in these animals ranged from 90 to 120 min. (mean 110 min.) in the 5 animals studied. The bowel appeared normal both radiographically and at autopsy in 4 of these 5 rats. In a single rat (No. 42, *Table VI*) a dilated loop of intestine was seen in the radiograph taken at 90 min., and at autopsy there was

Table VI.—Radiological Appearances and Post-mortem Findings in Rats subjected to Division and Re-suture of the Small Intestine Distally

Rat No.	Site of Division and Re-suture	Radiological Appearances			Post-mortem Findings	
		Time after Operation	Intestinal Transit Time (min.)	Anatomy	Time after Operation	Anatomy
38	Junction of middle and lower third of small intestine	2 mth.	90	Normal	4 mth.	Normal. A few adhesions surrounding anastomosis
39	Ditto	2 mth.	120	Normal	7 mth.	Normal
40	Ditto	2 mth.	120	Normal	7 mth.	Normal
41	Ditto	2 mth.	120	Normal	7 mth.	Normal. A few adhesions at site of anastomosis
42	Ditto	2 mth.	120	Slight enlargement of a loop of intestine in one film	7 mth.	Adhesions at site of anastomosis causing partial obstruction. Intestine slightly enlarged for 2 in. proximal to this point. Distal intestine normal
		Mean = 115 min.				

an adhesion which partly obstructed the bowel at the site of anastomosis, with hypertrophy of the bowel for 2–3 in. above this point.

5. Histology.—The histological appearance of normal rat intestine and an example of the enlarged distal intestine following resection of the proximal small intestine are shown in *Fig.* 455 A, B. The histology of normal rat intestine which has been distended by the injection of fluid to the calibre of the enlarged distal intestine is illustrated in *Fig.* 455 C.

The histological appearances suggest that the enlargement of the distal small intestine following proximal resection is not merely due to dilatation but is a true hypertrophy of both mucosal and muscular layers. The muscle wall of the enlarged distal intestine is greatly thickened when compared with the normal and the mucosa shows hypertrophy of the villi (*Fig.* 455).

A B C

FIG. 455.—A, Histological section of small intestine from normal rat. B, Section showing hypertrophy of mucosa and muscle coat of distal small intestine following proximal resection. C, Thinning of all coats of normal small intestine distended by injection of fluid; contrast with B.

DISCUSSION

The results show that there is a striking difference between the effects produced by resection of the proximal or the distal small intestine in rats.

Effect of Resection on Intestinal Transit Time.—When the *distal* intestine has been resected, the mean rate of passage of barium from the stomach to the colon is two to three times more rapid than normal, and the increase in transit time is roughly proportional to the amount of distal intestine which has been resected (*Tables III, IV*). After resection of comparable amounts of *proximal* intestine on the other hand, the intestinal transit time remains normal (*Tables I, II*). These results confirm previous observations that the rate of transit through the proximal intestine is very much more rapid than through the distal small bowel (Reynell and Spray, 1956; Booth, 1958).

Effect of Resection on Anatomy of Intestine.—Resection of the *distal* small intestine appears to have no material effect on the anatomy of the remaining small intestine. Even when as much as two-thirds of the distal intestine is resected, there is usually no change in the anatomy of the bowel unless adhesions cause partial obstruction at the site of the anastomosis (*Tables III* and *IV*). In such cases there is some hypertrophy of the small intestine but only for 1–2 in. immediately proximal to this point. In contrast to these results, resection of the *proximal* small intestine is followed by striking changes in the anatomy of the small intestine *distal* to the site of anastomosis. When approximately two-thirds of the small intestine is removed proximally, there is invariably gross enlargement of the distal small intestine, although the remnant of the proximal intestine remains normal (*Fig.* 454 A, B; *Table II*). These changes occur as early as six weeks after operation. Similar observations were made in the rats in which one-third of the proximal small intestine was resected, but the changes in these animals occur less consistently and take a longer time to develop. Of 2 animals subjected to these resections which were X rayed at six weeks after operation, the small intestine was normal in one and showed only slight enlargement of the distal small intestine in the other (*Table I*). Furthermore, the small intestine was found to be normal in 1 of the 5 animals killed six months after the operation, and in the remaining 4 rats the enlargement of the distal small intestine was less marked than in the animals subjected to the more extensive resections.

Nature of the Intestinal Hypertrophy.—The histological appearances of the enlarged distal intestine show that the changes are due to a hypertrophy of the mucosal and muscle coats of the distal small intestine (*Fig.* 455). The nature of this hypertrophy is uncertain. It is not merely due to interference with the continuity of the small-bowel wall, since simple division and re-suture of the bowel does not produce such changes (*Tables V, VI*).

Many workers have concluded that partial resection of the small intestine is followed by hypertrophy which is 'compensatory' for loss of functioning intestinal cells, and is comparable to that which may occur following loss of tissue in organs such as the liver or kidney (Jackson, 1958). The evidence, however, is conflicting. Such 'compensatory hypertrophy' of the remaining small intestine has been reported following massive resection of the small intestine in the dog by Senn (1887), Flint (1912), and Stassof (1914), and by Barker (1905), West, Montague, and Judy (1938), and Althausen, Vyeyama, and Simpson

(1949) in man. On the other hand, Jensenius (1945), in an extensive and careful study, found no evidence of intestinal hypertrophy following either proximal or distal resection in the dog, and in man hypertrophy of the remaining intestine does not invariably follow massive resection (Shonyo and Jackson, 1950; Shetton and Blaine, 1954). The observations reported in this paper show that intestinal hypertrophy may follow resection of the *proximal* small intestine in the rat. This hypertrophy, however, is apparently not 'compensatory' for loss of length of the small intestine, since hypertrophy does not follow resection of comparable lengths of distal small intestine. Furthermore, the hypertrophy does not involve the remnant of the proximal bowel which remains after a proximal resection (*Figs.* 453, 454; *Tables I, II*).

An alternative explanation for this hypertrophy is suggested by the observations of Kennedy and McCance (1958), who have reported the effect of dietary bulk in the rat. Rats given a mixture of 3 parts of powdered kaolin to (or with) 1 of their normal diet maintain their dietary requirements by eating a far greater bulk than when given a non-diluted diet, and such rats show enlargement of the gut to four times its usual size. This dilatation is presumably caused by the large bulk of unabsorbed kaolin within the intestinal lumen. A similar mechanism might explain the enlargement of the distal small bowel following proximal resection reported in this paper. Resection of the proximal intestine removes an area which is actively concerned with the absorption of food and with reduction in volume of the chyme as it passes down the lumen of the small intestine (Verzár and MacDougall, 1936). After proximal resection the volume of chyme delivered to the distal small bowel, whose inherent motility is sluggish, is very much greater than in the normal animal with an intact and absorbing proximal intestine. In these circumstances hypertrophy might be expected to occur in order to accommodate the larger volume of intestinal contents which reaches the distal intestine, whereas resection of the distal intestine would produce no such result. This hypothesis also explains the observation that the amount of proximal intestine resected determines the rapidity of onset and degree of enlargement of the distal small intestine (*Figs.* 453, 454; *Tables I, II*). The effect of dietary bulk on the calibre of the intestine is being studied further in normal rats and in those with partial resection of the small intestine.

SUMMARY

Radiographic and post-mortem studies were carried out in groups of rats which had been subjected to resection of one-third or two-thirds of the proximal or distal small intestine, and in similar groups of rats in which the intestine was simply divided and re-sutured.

After *proximal* resection, the intestinal transit time was similar to that in normal rats. Anatomically, however, there was moderate or gross enlargement of the intestine *distal* to the site of anastomosis in these animals.

In contrast, when the *distal* intestine was resected, the intestinal transit time was two to three times more rapid than in normal rats. The remaining intestine, however, showed no evidence of hypertrophy unless there was obstruction at the site of anastomosis.

The enlargement of the distal intestine following proximal resection was due to a hypertrophy of both mucosal and muscle coats. The pathogenesis of this hypertrophy is discussed.

Acknowledgements.—We wish to thank Dr. R. E. Steiner, Dr. J. W. Laws, Mr. R. Shackman, and Dr. I. Doniach for their encouragement and advice; Mr. Casimir Milczek for his assistance with the handling of the experimental animals; and Mr. Brecknell and the staff of the photographic department for the reproductions.

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SHORT NOTES OF RARE OR OBSCURE CASES

TENSION PNEUMOPERITONEUM

A REPORT ON TWO CASES

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PNEUMOPERITONEUM can be produced by infection of the peritoneal cavity with a gas-producing organism, but the more common cause is due to perforation of a viscus, and if there is a valvular closure of this perforation a tension pneumoperitoneum may result.

Two examples of gas under pressure in the abdomen, caused by a perforated peptic ulcer, are recorded.

CASE REPORTS

Case 1.—J. L., a retired labourer aged 67 years, was admitted to hospital with a distended abdomen, on Feb. 16, 1957. One year previously a gastro-enterostomy had been performed for pyloric stenosis caused by a very large œdematous ulcer in the juxta-pyloric region, and he had been well, except for bronchitis, until 5 days before admission. He gave a history of 5-days' abdominal pain, which had started in the epigastrium, spread over the whole of the abdomen, and was associated with a feeling of fullness and gradual increase in abdominal girth. He had felt sick but had not vomited, bowels and micturition being normal. He had become increasingly breathless the day prior to admission.

ON EXAMINATION.—A very ill cyanosed old man, with a blood-pressure of 110/60 mm. Hg, pulse-rate 120 per min., temperature 99° F., and respirations 50 per min. The abdomen was grossly distended and tympanitic all over, with a little epigastric tenderness. Rectal examination was negative. On auscultation a few faint bowel sounds were heard.

A vertical plain film of the abdomen showed the presence of free gas throughout the peritoneal cavity. The large bowel appeared slightly distended, but there were no fluid levels (*Fig.* 456). Diagnosis of tension pneumoperitoneum was made.

TREATMENT.—In view of the poor general condition of the patient a conservative régime was decided upon. He was given sedatives and antibiotics and put on gastric suction and intravenous fluids. In order to relieve the abdominal distension, a wide-bore cannula was inserted into the peritoneal cavity through the lower part of the linea alba. A large amount of odourless gas escaped under tension. The distension disappeared almost immediately, and the condition of the patient improved, the respirations being less laboured. Twelve hours later his abdomen was again distended and a further decompression was carried out, but his condition deteriorated rapidly and he died 36 hours later.

AT AUTOPSY (Dr. W. Goldie, St. James's Hospital).—"The peritoneal cavity contains a great quantity of thin yellow fluid. There is a generalized peritonitis with fibropurulent adhesions between adjacent coils of small intestine, which were slightly distended. Immediately distal to the gastro-enterostomy stoma, on the jejunal side of the loop, is a small opening, 0·5 mm. across, which is a perforated stomal ulcer. In the stomach is a chronic pyloric ulcer which is benign."

It is interesting to note the development of a jejunal ulcer at the age of 67 years, following gastro-enterostomy for pyloric stenosis caused by an enormous active ulcer. This shows that gastro-enterostomy for pyloric stenosis is never sure to avoid this complication of anastomotic ulceration.

Case 2.—W. J., a clerk aged 46 years, was admitted to hospital a month after *Case* 1. He gave a history of 36-hours' generalized abdominal pain and swelling of the abdomen. The pain had come on gradually and was

FIG. 456.—*Case* 1. Vertical plain radiograph of abdomen demonstrating tension pneumoperitoneum and showing outlining of abdominal wall and walls of intestine.

fairly severe on admission. He had not vomited, and his bowels had been opened the previous day. He had suffered from indigestion for 4 years, had a poor appetite, and had lost some weight during the previous 6 months.

ON EXAMINATION.—The patient looked pale and anxious and was having difficulty in breathing. The pulse-rate was 150 per min., temperature 98·2° F., and respirations 56 per min. The abdomen was grossly distended, tympanitic, and tender all over. Rectal examination revealed tenderness in the recto-vesical pouch.

A vertical plain film of the abdomen showed a large amount of free gas in the peritoneal cavity (*Fig.* 457). A lateral film illustrated a huge gas shadow under the anterior abdominal wall (*Fig.* 458). Diagnosis of tension pneumoperitoneum was made.

AT OPERATION.—Before a general anæsthetic was administered the abdominal distension was relieved by the insertion of a wide-bore cannula into the peritoneal cavity, when odourless gas under tension was released. Following decompression the patient's breathing became easier and his general condition improved. Ten minutes

later the abdomen was explored through a right upper paramedian incision. The upper abdomen and pelvis contained a thin turbid effusion, which was removed by suction. High up on the lesser curvature of the stomach was a large perforated gastric ulcer, which had everted

FIG. 457.—*Case* 2. Vertical plain radiograph of abdomen showing tension pneumoperitoneum.

edges and felt malignant; the left lobe of the liver was lying directly over the ulcer. The perforation was closed with catgut sutures and covered with omentum. The abdomen was closed in layers with pelvic drainage through a suprapubic wound.

The patient made a fairly rapid recovery in the first two weeks, but after this suffered repeated hæmatemeses which necessitated massive blood transfusions. Further surgical treatment was refused, yet he survived.

DISCUSSION

Both these cases presented were sent into hospital with a provisional diagnosis of intestinal obstruction, and it is from this condition that tension pneumoperitoneum must be distinguished. If accumulation of air in the peritoneal cavity is excessive, this leads to ballooning of the abdomen, which is barrel-shaped and tympanitic all over, even in the loins. In the later stages the diaphragm is displaced upwards, leading to laboured respiration, cyanosis, and tachycardia. The patient feels full and distended, though fairly comfortable, and only complains of pain if a peritonitis develops. The lack of vomiting, severe pain, and the persistence of peristaltic sounds help to differentiate the condition from intestinal obstruction. A straight radiograph of the abdomen is diagnostic, as air is seen in the abdominal cavity outlining the parietes, solid structures, and the walls of the intestine.

All these diagnostic features were described originally by Singer (1932), who recorded 4 cases. One of these was due to a perforated peptic ulcer, and the other 3 due to perforated stercoral ulcers of the cæcum. When his cases were operated upon, odourless gas escaped under tension. He points out that only if a large volume of air escapes alone and there is little or no extravasation of liquid material to cause a peritonitis, does a true tension pneumoperitoneum result. In non-valvular pneumoperitoneum, as in a perforated peptic ulcer, the distension is mainly due to inflation of the intestinal loops caused by peritonitis, rather than to intraperitoneal air.

FIG. 458.—*Case* 2. Lateral plain radiograph of abdomen showing huge gas shadow under anterior abdominal wall.

In the second case described here, it is suggested that the lobe of the liver lying over the ulcer may have produced a valvular effect.

In the advanced stages of a true tension pneumoperitoneum decompression of the abdomen may be a life-saving procedure. This is well illustrated by Conole and D'Angelo (1952), who describe the spontaneous development of this condition following the resection of a pharyngeal diverticulum. Their patient recovered rapidly following laparotomy and the release of gas under pressure.

In the management of this rare condition, decompression by aspiration appears to be the first procedure to improve the general condition of the patient, as a rapidly developing pneumoperitoneum can be fatal. This should be followed by an exploratory laparotomy, as closure of a perforated viscus is essential, especially if there are signs of a supervening peritonitis.

Acknowledgements.—I wish to thank Mr. H. S. Shucksmith for permission to publish *Case* 1, and for his helpful criticism; my thanks are also due to Mr. M. C. Oldfield for permission to publish *Case* 2, and to Dr. W. Goldie for performing the autopsy.

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BILATERAL SYNCHRONOUS POSTERIOR DISLOCATION OF THE SHOULDER

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UNILATERAL posterior dislocation of the shoulder is a well-recognized, if uncommon, injury. Bilateral posterior dislocations, however, are rare; only 9 previous cases could be found in the literature.

A further bilateral case is here recorded which was successfully treated by immediate manipulative reduction; the diagnosis of the condition and the mechanism of injury are discussed.

FIG. 459.—Right shoulder. Humeral head internally rotated with a compression fracture of the anteromedial aspect with flakes of bone below the glenoid.

FIG. 460.—Left shoulder held similarly in internal rotation, with a less severe compression injury of the humeral head

CASE REPORT

J. G., aged 46 years, a labourer, suddenly lost consciousness while working on a building site on Jan. 24, 1957, and is reported to have fallen backwards on to a pile of boards. He regained consciousness in a few seconds and at once experienced pain in both shoulders. Examination of the patient 2 hours later showed that he was a broad, exceptionally muscular man, who held both arms adducted and internally rotated at the shoulders; there was no obvious visible deformity and no bruising of the arms or back suggestive of severe trauma. Palpation of the shoulders revealed an indistinct mass posteriorly on both sides, and a hollow was discernible anteriorly on the left. No external rotation was possible at either shoulder and all scapulo-humeral movements were markedly limited.

The patient had a hypertension of 200/110 mm. of mercury. No other cause for his loss of consciousness could be found.

Anteroposterior radiographs showed that both humeral heads were internally rotated and that there were defects on their medial aspects with small adjacent bone flakes (*Figs.* 459, 460). The appearances suggested bilateral posterior dislocation, and axial views were then taken to elucidate the bone defects and to confirm the displacement of the heads. These views suggested that the defects were, in fact, caused by severe impaction of the humeral heads against the posterior margins of the glenoid fossæ.

That evening, under general anæsthesia, both dislocations were reduced by manipulation (*Fig.* 461). Traction in abduction and external rotation were employed. The reductions were stable in all positions including internal rotation, and after reduction collar-and-cuff slings and a body bandage were applied.

A month after the injury the bandage and all supports were discarded and the patient returned to his job as a heavy manual labourer. A month later he had full painless function of both shoulders.

DISCUSSION

Diagnosis.—The literature reveals how frequently posterior dislocations of the shoulder have eluded early diagnosis, even with the help of radiography. Of the bilateral dislocations previously recorded only one was diagnosed at the first examination.

The full and rapid recovery of function in our patient following early manipulative reduction stresses the importance of early diagnosis. The most striking clinical feature of the present case was the fixed internal rotation of the upper limbs. The

absence of any visible deformity, coupled with the difficulty of palpating the bony structures, in a man whose shoulder musculature was exceptionally well developed, left the diagnosis in some doubt. The radiographic examination enabled a confident diagnosis to be made. The axial views, although not of reproducible quality, were obtained in this case with little discomfort to the patient. When the few degrees of abduction at the shoulder necessary for this projection cannot be obtained without pain the nature of the dislocation can be confirmed by lateral transthoracic views, an interruption in the normal smooth arch formed by the lateral margin of the scapula, and the medial margin of the shaft and neck of the humerus being seen when there is a posterior dislocation (Dorgan, 1955).

FIG. 461.—Right shoulder after reduction.

Mechanism of Injury.—Three possible explanations have been offered for the way in which unilateral posterior dislocation may occur:—

1. Direct violence to the front of the shoulder (Taylor and Wright, 1952).

2. A fall on to the hand with the arm flexed and adducted at the shoulder (Taylor and Wright, 1952; McLaughlin, 1952).

3. Forcible internal rotation at the shoulder from a fall on the arm (Michaelis, 1950).

It is evident that none of these suggested mechanisms can account for cases of simultaneous bilateral posterior dislocation occurring in the absence of external trauma, and as will be seen from *Table I*, the majority of bilateral cases in which the aetiology was known occurred during convulsive seizures. In such cases the only feasible mechanism would seem to be violent contraction of the shoulder-girdle muscles. The violence of this pull is indicated by the degree of impaction injury which the humeral head may receive from the posterior rim of the glenoid (*Fig.* 459). In the present case the severity of this impaction injury was exceptional and can, in our opinion, be accounted for by the unusual degree of muscular development due to the patient's occupation.

Unilateral cases also occur following epileptic seizures and in many of these it would seem likely that the cause of the dislocation is the same as in the bilateral cases. Mynter (1902) reported the occurrence of a posterior dislocation during a fit suffered while the patient was in bed, and we have seen such a dislocation which occurred during an epileptic convulsion, under circumstances in which external violence of the severity required to produce a dislocation could be discounted.

SUMMARY

A case of bilateral posterior dislocation of the shoulders is reported and the diagnosis and

Table I.—PREVIOUS REPORTS OF BILATERAL POSTERIOR DISLOCATION OF THE SHOULDER

AUTHOR	DATE	CAUSE	DELAY IN DIAGNOSIS	MANIPULATIVE REDUCTION	FURTHER TREATMENT	REMARKS
Coover	1932	Epileptic seizure	3 weeks	Failed	None	
Möllerud	1946	No cause discerned	2 years		No treatment	A case of habitual bilateral posterior dislocations of long standing
Wilson and McKeever	1949	Epileptic seizure	12 days	Failed	Open reduction	Good result both sides
McLaughlin	1952	Unknown	35 years	Not attempted	None	
		Epileptic	Several years	Not attempted	None	Initially recurrent dislocations. Later became fixed
Dorgan	1955	Motor accident	Immediate diagnosis	Successful	None	The only recorded instance of the dislocations following upon major external violence
		Unknown	Unknown period	Not attempted	Open reduction	
Arden	1956	Epileptic seizure	3 weeks	Failed	Open reduction	Good result both sides
O'Connor and Jacknow	1956	Epileptic seizure	1 week	Not attempted	Open reduction	Good result both sides

mechanism of injury are discussed. A table of the previously reported cases is included.

We are grateful to Mr. J. C. Scott, Director of the Accident Service at the Radcliffe Infirmary, for permission to publish this case.

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ABDOMINAL SPLENOSIS FOLLOWING RUPTURE OF THE SPLEEN IN A BOY AGED 10 YEARS

BY R. B. ZACHARY AND JOHN L. EMERY
FROM THE CHILDREN'S HOSPITAL, SHEFFIELD

ABDOMINAL symptoms due to growth of autogenous implants in the peritoneum following rupture of the spleen are extremely uncommon. The following case is reported because of its rarity and the confusing symptomatology that preceded diagnosis.

CASE REPORT

A. L., a boy 12 years of age, had two younger sisters who were quite well. Two years before being seen at the Sheffield Children's Hospital, then aged 10, he had been sledging and had sustained an injury to the abdomen, causing a ruptured spleen which was removed. Two months later, after being perfectly well, he was suddenly doubled up with abdominal pain which lasted for over 3 hours and left him just as suddenly as it had come on. For the next 18 months he was perfectly well, although sometimes his stools were hard and he had abdominal discomfort, but there was no real attack of abdominal pain. There was some headache during this time, for which the maxillary sinuses were considered to be responsible and the left maxillary sinus was irrigated.

In September, 1956, about 20 months after the splenectomy and 2 days after returning to school following the summer holidays, he had a severe abdominal pain which continued all night and all the following day. He was admitted to hospital and his appendix was removed the same evening. At operation it was said that there were many adhesions and that the appendix was inflamed.

About 2 months after appendicectomy he was suddenly struck by a similar bout of abdominal pain which lasted 6 or 7 hours and then gradually subsided during the next 12 hours, and from that time the recurrent abdominal pain was very severe and was uninfluenced by sedatives or by probanthine. Clinical examination revealed a somewhat obese boy who did not appear to be ill. There were no abnormal physical findings except the two abdominal scars, one for the splenectomy and one for the appendicectomy.

No firm diagnosis was made at that time. The intravenous pyelogram was normal; barium meal and follow-through showed no abnormality. Although there was no doubt some psychological overlay, it was not considered that this was primarily a psychological problem, or an example of abdominal migraine or epilepsy.

The pain persisted in spite of ensuring that the stools were soft, and on one visit to hospital the patient was so persistent in localizing the abdominal pain to the lower part of the right paramedian scar that it was decided to explore the abdomen. Operation on July 11, 1957, through the previous right paramedian scar, revealed one large and some small red swellings on the wall of the ileum 9 in. above the ileocæcal valve. The total distance involved by these swellings was about 3 in. A portion of terminal ileum measuring about 9 in. was resected and an end-to-end anastomosis performed. The post-operative course was very smooth and the boy has had no further abdominal pain since then.

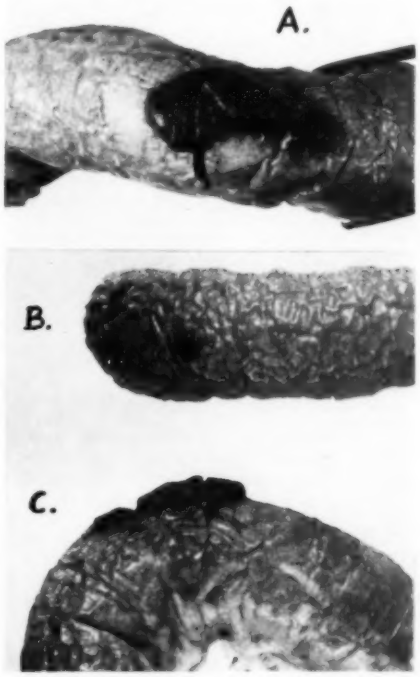

FIG. 462.—Photograph of excised bowel (× 2·3) showing the splenic autotransplants. A and C are different views of the larger lesion, B shows the multiple small lesions nearby.

BIOPSY.—Approximately 25 cm. of small bowel had been resected. The bowel showed uniform contour with

no areas of constriction or hypertrophy. The mesentery appeared normal. Along the line of the bowel furthest away from the mesentery were a series of 5 deep red masses, superficially looking like cavernous hæmangiomas. The edges stood out almost at right angles to the peritoneal surface (*Fig.* 462). The largest mass was pear-shaped, being approximately 2 cm. long and 1 cm. wide. The other masses were much smaller, being almost circular

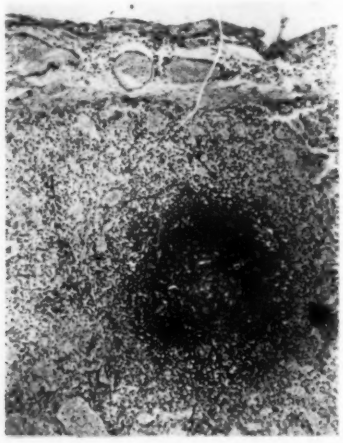

FIG. 463.—Photograph of a section of the tumour mass showing Malpighian bodies, pulp, and the fibrous capsule covered by peritoneum. H. and E. (× 47.)

and 1–3 mm. in diameter. Vessels on the serous surface leading to these masses were very prominent.

No abnormality could be seen in the underlying mucous membrane and the Peyer's patches, although easily identified, were normal.

Microscopy (*Fig.* 463) showed that the masses were splenic tissue with normal follicles and pulp. The only difference from normal spleen was that the masses were surrounded by connective tissue in which smooth muscle-fibres were not identified.

The whole masses were completely outside the muscular wall of the gut, and appeared to be in the substance of the visceral peritoneal membrane.

DISCUSSION

The history and anatomical findings in this case are typical of abdominal splenosis. The literature of the condition has been well reviewed by Jarcho and Andersen (1939) and more recently by Storsteen and ReMine (1953). Approximately 25 cases of the condition have been reported. The only one that we have been able to find in this country is that described by Lee (1923). His patient had a laparotomy for intestinal obstruction at the age of 29 years; splenosis was found and it was learned that the spleen had been removed after injury at 14 years of age. In 18 of the reported cases, 11 had sustained the splenic trauma before the age of 15 years, and only 5 after the age of 20 years. The latent period between the date of rupture and laparotomy varied from 1 to 36 years. Experimental work suggests that the splenic autotransplants grow from the reticulum cells of the spleen exclusively (Calder, 1939), and this may explain the absence of smooth muscle in the implants.

A history of trauma was obtained in almost all of the recorded cases, but in a few no definite story of injury is reported. We think the history in these cases must be incomplete or inaccurate, and that trauma is an essential prerequisite for the development of abdominal splenosis. Certainly the condition has not been reported to follow simple splenectomy for other conditions (Shaw and Shafi, 1937).

The cause of intestinal colic in some cases is uncertain. In some cases the appendix has been reported as "inflamed"; in others a band has been divided and one or two of the larger nodules removed, with relief of symptoms. In this present case no other cause of symptoms was found, and the patient's severe pain ceased following resection of the portion of bowel most obviously affected. The transplants do not encroach on the lumen of the bowel and are quite external to the muscle-fibres. They are soft, and the only explanation that seems likely to us is that the sheaf of vessels running to the implant around the bowel in some way interfere with peristalsis and cause a reflex band of spasm. We have found no case report where a second laparotomy has been required even though hundreds of implants were present in the peritoneal cavity. Although some consider that the growth of splenic tissue is not compensatory to the removal of the spleen (Shaw and Shafi, 1937), the experimental work of Cameron (1957) would suggest that implants grow only until the total bulk of the implant material has reached the size of the original spleen. At that point they remain stationary. The implants apparently grow rapidly, and on that basis, any symptoms likely to be produced would be expected to be early, and provided the actual offending lesion is removed at operation, recurrence of symptoms would appear to be unlikely.

Acknowledgement is made to Mr. R. Cousins and Mr. C. P. J. Rickus for the photographs.

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REPORT OF A CASE OF INTESTINAL OBSTRUCTION DUE TO RENAL CALCULUS

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It has long been known that intestinal obstruction may be caused by gall-stones ulcerating through into the duodenum, but no reference is made to obstruction due to renal calculi in text-books of surgery and we have only been able to trace one other reported case (Krüger, 1954).

The following case is reported as an extreme rarity.

CASE REPORT

Mrs. M. P., aged 74, was admitted on March 21, 1957, complaining of colicky abdominal pains for four days and vomiting for twenty-four hours; her description of the vomit suggested fæcal vomitus. Her bowels had always been regular but had not acted for twenty-four hours. She denied any disturbance of micturition. Her weight was steady. There was nothing of significance in her past history.

On Examination.—The patient was a fairly fit old lady, temperature 98° F., pulse 90 per min., respirations 24 per min. Her tongue was moist and clean and there was no evidence of dehydration. Blood-pressure was 200/110. There was nothing abnormal in her cardio-vascular or respiratory systems. Her abdomen showed slight central distension but there was no visible peristalsis. There was a mass in the right loin which moved with respiration. Bowel sounds were increased and obstructive in character. Routine examination of the urine showed nothing abnormal.

A diagnosis of intestinal obstruction due to a carcinoma of hepatic flexure was made. Straight radiography of the abdomen confirmed small bowel obstruction but showed no distended cæcum. An opacity, which later proved to be the stone, was seen in the pelvis and was reported as being a bladder calculus.

At laparotomy on March 22, 1957, distended small bowel was seen, but the cæcum and terminal ileum were collapsed. Following the distended bowel downwards obstruction was found to be due to a large stone, resembling a broken staghorn calculus, in the lower ileum. This was removed and the bowel closed. The gall-bladder and stomach were normal. The mass in the right loin proved to be a large kidney, and there were a few inflammatory adhesions around the region of the hepatic flexure.

The patient made an uneventful recovery and was discharged on April 8, i.e., the seventeenth post-operative day. During her convalescence an intravenous pyelography was performed, showing a non-functioning right kidney with a few pieces of stone remaining within the renal shadow.

The stone measured 6 × 4 cm. and weighed 41·5 g. (*Fig.* 464). Analysis showed the outer part to consist of phosphate and carbonate, whilst the core consisted of oxalate and phosphate with only a trace of carbonate. Tests for cholesterol and uric acid were negative.

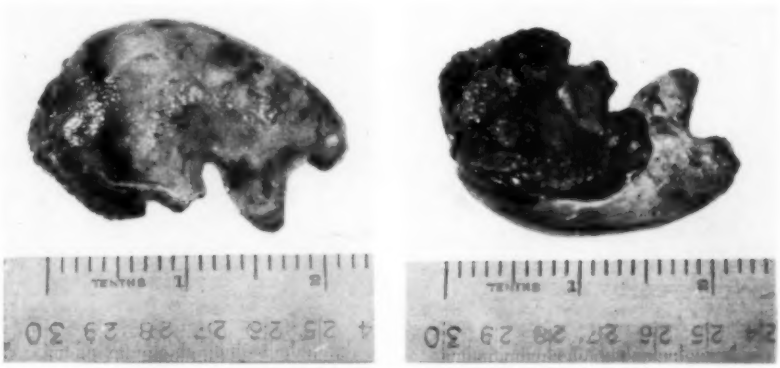

Fig. 464.—Stone removed from terminal ileum.

The patient was last seen in the out-patient department on May 22, 1957, when she was very well. At this attendance she admitted to some pain in the right loin for many years, but said that this had now improved. The mass was still present, much the same size, and not tender. In view of her age and in the absence of symptoms, we considered that nephrectomy was not indicated.

DISCUSSION

We can only surmise that this stone ulcerated through from the renal pelvis into the second part of the duodenum, in which case one must assume that the renal vessels thrombosed before the ulceration occurred, as there was no evidence of bleeding in this region.

In Krüger's case (1954) the patient presented as a case of pyloric stenosis; at operation the stone was found in the upper jejunum and the duodenum was large and inflamed. This patient died on the fourth day and at post-mortem examination an atrophic right kidney with a fistula admitting a thumb was found between the renal pelvis and the duodenum. No mention was made of the state of the renal vessels. It is interesting that this stone was almost

exactly the same size as in the present case—6 × 4 × 2 cm.

SUMMARY

A case of intestinal obstruction due to a renal calculus is presented. Only one other such case can be traced, which showed that ulceration had occurred between the renal pelvis and duodenum.

Acknowledgements.—Our thanks are due to Mr. R. Conroy, who took the photographs, and to Mrs. Collison, who typed the manuscript.

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ENLARGED LYMPHATIC GLANDS IN A CASE OF MULTIPLE PIGMENTED NÆVI

BY T. J. S. PATTERSON, OXFORD

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THE occurrence of malignant melanoma before puberty is rare, and the occurrence of malignant change in large pigmented nævi is rarer still. At the Hospital for Sick Children, Great Ormond Street, during the years 1930–52, 390 malignant tumours were seen; of these, 3 were malignant melanomata, none of which arose from large pigmented nævi (Bodian and White, 1952).

FIG. 465.—Child, aged 13 months. Multiple pigmented nævi before surgical treatment.

There is no definite evidence to suggest that interference with a pigmented lesion predisposes to malignant change. It seems more likely that such lesions are already malignant by the time treatment is sought (Cade, 1957). With these facts in mind, large pigmented nævi are now commonly treated before puberty by partial excision, either in full thickness by serial excisions, or in partial thickness by shaving or planing.

Nevertheless, any surgeon who treats these cases must watch some of them with anxiety when he sees excessive production of pigment or the disordered histological picture of the juvenile melanoma.

This case report describes a child with multiple pigmented nævi and a very extensive deeply pigmented lesion of the trunk, with enlarged axillary and inguinal glands which were black.

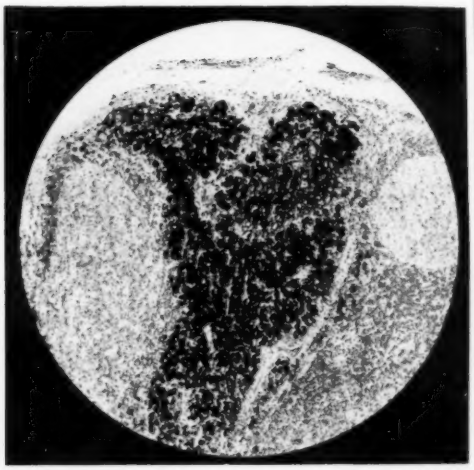

FIG. 466.—Lymphatic gland. (× 54.) Peripheral sinus containing melanin.

CASE REPORT

This girl, now 8 years old, was born eight weeks prematurely with a large deeply pigmented nævus of the trunk and scattered smaller patches over the rest of her body (*Fig.* 465).

The greater part of the first two years of her life was spent in hospital owing to the intense irritation produced by the lesion on her trunk. The surface repeatedly ulcerated due to her scratching, and she required heavy sedation. The surface was hard and nodular and the skin was very thick and inelastic. No hairs grew on the pigmented area. In addition there were many pigmented patches over the rest of the trunk and the limbs. The head and neck were spared, apart from the scalp and one patch on the lower lip and one on the hard palate. The lymph-glands of the axillæ and groins were markedly

enlarged, discrete, and mobile. The largest glands were in the right groin.

Biopsy of the right groin and the left axilla showed the glands to be fleshy and deeply pigmented (*Fig.* 466).

FIG. 467.—Child, aged 3, during surgical treatment.

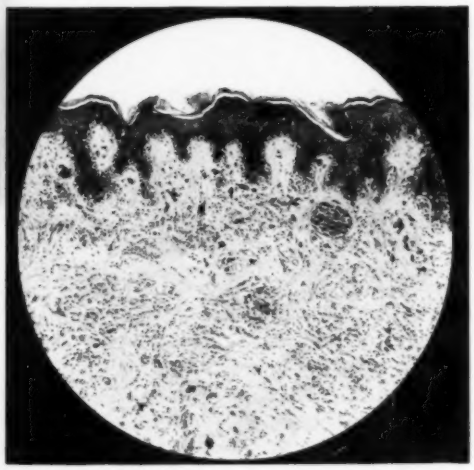

FIG. 469.—Pigmented nævus of trunk. (× 54.) (*See* histological report in text.)

HISTOLOGICAL REPORT.—"All the lymph-nodes show comparable changes, that is, a follicular simple hyperplasia, but there is no evidence of neoplastic change. Some peripheral sinuses contain appreciable quantities of melanin."

Surgical treatment was started in 1952, when the child was 2½ years old. Over the next three years twelve operations were carried out on the trunk. Serial excisions, free grafts, and local flaps were used until the greater part of the lesion had been removed (*Fig.* 467). Since the skin of all available donor areas was covered with

FIG. 468.—Child, aged 8. The greater part of the lesion on the trunk has been removed, but pigmented patches have been transferred with the skin grafts.

pigmented patches, some of these were inevitably transferred to the recipient areas on the trunk (*Fig.* 468). As the size of the lesion was reduced the axillary and inguinal glands became smaller until they are now within normal limits. Repeated histological examination of the pieces removed showed a constant picture (*Fig.* 469).

"The epidermis is irregularly thickened and is heavily pigmented. There is some junctional activity.

"The dermis is considerably thickened and there has been extensive replacement of the normal fibro-fatty tissue by dense collagen. The sub-epithelial tissues contain large numbers of nævus cells. These form rounded or irregularly shaped alveolar masses or else are arranged in narrow trabeculæ; the individual cells are strikingly uniform in appearance and mitotic activity is minimal.

"In the deeper parts of the specimen many of the small veins contain subintimal collections of nævus cells. Some nævus cells lie in close relation to vessels, but there is no evidence of invasion of either blood or lymphatic channels.

"There is no evidence of malignancy."

Comment.—In spite of the sinister clinical appearance there has never been any histological evidence of malignancy in the glands or in the excised skin. This is borne out by the condition of the child, who is now 8 years old and is in excellent health.

In the commoner type of large pigmented nævus where the skin is brownish, of good texture, and hairy, irritation is not a problem. In the less common type such as that described above where the skin is deeply pigmented, thickened, and hairless, irritation may be intense and makes surgical treatment a matter of some urgency as soon as the child is old enough to withstand grafting operations.

SUMMARY

A case is described of multiple pigmented nævi in a child. The axillary and inguinal glands were enlarged due to excessive pigment production by a very large lesion on the trunk. This was excised in stages and the glands became progressively smaller.

Acknowledgements.—I wish to express my thanks to Professor Moncrieff for permission to report this case, and to Mr. D. N. Matthews, under whose care the surgical treatment was carried out, for help in the preparation of this paper. Dr. Martin Bodian has very kindly provided the histological reports. The photographs are the work of Mr. Derek Martin at the Hospital for Sick Children.

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BENIGN GRANULAR-CELL MYOBLASTOMA OF THE BRONCHUS

BY E. R. JONES AND A. M. MACARTHUR
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MYOBLASTOMA is a term used originally by Abrikosoff (1926) to describe tumours of the tongue and other structures, consisting of ovoid cells containing coarse acidophilic granules, and in some cases showing the striations and other features of voluntary muscle. After this initial report cases were described in which the tumour was found in various other parts of the body, such as the orbit, stomach, œsophagus, vulva, omentum, and larynx. The presence of a myoblastoma where there is normally no striped muscle has been explained by implicating the histiocyte or Schwann cell as the parent tissue. The origin and nature of the lesion have been much debated and, indeed, Willis (1948) regards lingual myoblastomas as degenerative or regenerative lesions of muscle-fibres and not as tumours at all. However, some of this confusion has been resolved by Stout's (1953) observations on 136 cases which he has subdivided into benign and malignant groups. Whatever their precise origin, the label is a convenient one for a group of tumours with a characteristic histological picture.

The occurrence of a myoblastoma in the bronchus is a rarity, there having been only 7 cases previously reported in the world literature and none from this country.

Kramer's (1939) case presented with an acute febrile illness associated with cough, sputum, and radiographic signs of a collapsed right lower lobe. At bronchoscopy a tumour was found occluding the right lower lobe bronchus, and was destroyed by diathermy in the course of several bronchoscopies. Kraus, Melnick, and Weinberg (1948) performed a pneumonectomy for a destroyed lung secondary to myoblastoma in the right main bronchus. Lowbeer (1953) reports a similar case with a left-sided tumour. Liebow (1952) mentions the finding of a myoblastoma in the left upper lobe in a negro, but gives no other details. Ramsey's (1955) case was similar to that of Kramer and was treated by bronchoscopic removal of the tumour. Peterson, Soule, and Bernatz (1957) report 2 cases, one an accidental finding in an asthmatic, the other causing bronchial occlusion with cyst-formation behind the obstruction. Resection of the basal segments of the right lower lobe was carried out.

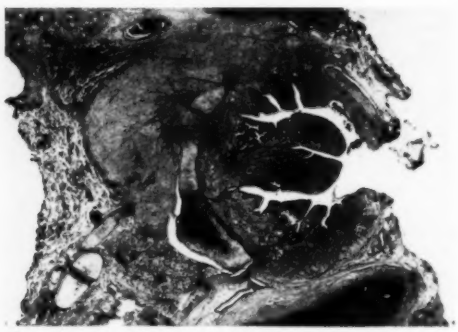

FIG. 470.—Bronchial granular-cell myoblastoma blocking the bronchus. (× 3·5.)

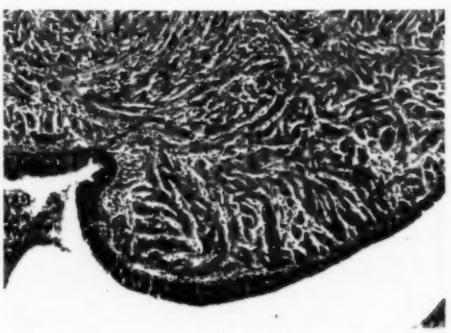

FIG. 471.—Higher magnification showing the granular cytoplasm of the component cells and syncytial masses, with a thin layer of connective tissue separating the tumour-cells from the epithelium. (× 50.)

CASE REPORT

H. H., female, aged 47 years, a heavy cigarette smoker, was referred to Preston Hall Hospital in July, 1956, with a history of two attacks of influenza, characterized by high fever, toxæmia, pain in the chest, and an unproductive cough. The first of these was in December, 1955, the second in March, 1956. In April, 1956, a radiograph showed consolidation of the apicoposterior segment of the left upper lobe. The patient had been treated with various combinations of antibiotics as a result of which her general condition improved and she became symptom-free. Further radiographs, however, showed the persistence of the consolidated segment, bronchoscopy revealed no abnormality, and tomography merely confirmed the presence of the consolidation. There were no malignant cells or tubercle bacilli in the sputum, the blood-picture showed no significant abnormality, and the E.S.R. (Westergren) was 21/2000 (1 hour). In view of the patient's age, history, and the radiographic appearances, it was thought likely that she was suffering from a bronchial carcinoma. Exploration was advised.

At thoracotomy on July 6, 1956, the apicoposterior segment of the left upper lobe was found to be consolidated and adherent to the chest wall. Several frozen sections from a large subaortic lymph-node revealed inflammatory changes only. As it was felt probable that the apicoposterior bronchus was obstructed by a tumour, a left upper lobectomy with an extensive dissection of the mediastinal structures from the apex of the pleura to the hilum was carried out. When the fresh specimen was examined a small polypoid tumour was found arising from the wall and completely blocking the lumen of the apicoposterior bronchus at its point of origin (*Fig.* 470).

On histological examination (Dr. E. R. Jones) this proved to be a granular-cell mybblastoma arising from the muscularis mucosæ. Bronchial mucosa adjacent to the tumour showed metaplasia with projections of a squamous cell epithelium extending into the depths of the tumour. In the collapsed lung segment there were chronic inflammatory changes with fibrosis, purulent bronchitis, and numerous small suppurative foci. The mediastinal and bronchial glands showed inflammatory changes and reactive hyperplasia only. Cytologically, the tumour was similar to those described by previous workers. It consisted of masses of large polyhedral cells with coarse granular acidophilic cytoplasm. In some parts there were ribbons of syncytial masses containing the same coarse granules (*Fig.* 471). Connective-tissue stroma was scanty, numerous groups of mucous glands were scattered throughout the tumour, and there were a few accumulations of lymphocytes present. No structures resembling striated muscle were seen. The patient made an uninterrupted recovery and was discharged 14 days later.

CONCLUSION

In none of the reported cases of bronchial myoblastoma has there been evidence of malignancy; all have had the characteristic histological picture found in this case and several have shown squamous metaplasia in the mucosa near the tumour. Clinically these tumours produce their effects by obstruction of a segmental, lobar, or main bronchus with distal suppuration and parenchymal destruction, the picture being indistinguishable from that due to other types of bronchial obstruction. The diagnosis is made by bronchoscopy and biopsy if the tumour is accessible. Treatment depends on the site of the tumour and the severity of the secondary changes. When the tumour shows infiltration of the bronchial wall, as in two of the reported cases, local removal should probably be by bronchotomy rather than via the bronchoscope. Where permanent lung changes have taken place resection of the damaged lung may be necessary, as was undertaken in 4 of the reported cases.

SUMMARY

Benign granular-cell myoblastoma is a rare cause of bronchial occlusion with obstructive pneumonitis. Such a case is described, and the seven others previously reported in the literature discussed.

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A COMPLICATION RESULTING FROM THE USE OF A RIGID INLAY IN THE REPAIR OF AN INGUINAL HERNIA

By PATRICK FITZGERALD
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AND J. E. MEHIGAN
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THE repair of an inguinal hernia by the use of a rigid inlay in the form of a silver filigree was described by McGavin in 1909. The method was criticized, but results compared favourably with other forms of treatment (Cole, 1941). When the hazards of sepsis were reduced by the advent of antibiotics, other materials for the inlay were introduced, e.g., tantalum gauze mesh (Throckmorton, 1948), and polythene plastic (Thompson, 1948). The latter was the material used in this case.

FIG. 472.—Aortogram demonstrating obstruction of right external iliac artery.

CASE REPORT

W. M., a 63-years-old postman, was admitted to St. Vincent's Hospital, Dublin, in April, 1956. He complained of intermittent muscular pain in the right thigh during exercise, relieved by temporary rest. His work as a rural postman involved, when on duty, cycling about 15 miles each day; recently severe pain had prevented him from doing this.

The only significant point in his previous history was the repair of a right inguinal hernia five years previously in another hospital, and there was no recurrence.

ON EXAMINATION.—No pulse could be felt in the femoral or distal arteries; oscillometry confirmed this. The arteries elsewhere were normal for a man of his age.

There was an obstruction in the right external iliac artery which was confirmed by aortography (*Fig.* 472). On radiography the collateral circulation appeared satisfactory. It was decided to excise the obstructed artery and insert a homologous arterial graft. The right external iliac artery was exposed through an oblique inguinal incision and at the same time the inlay was removed. It was obvious that the inlay compressed the external iliac artery during flexion of the thigh.

The obstructed artery was excised (*Fig.* 473) and replaced by an arterial graft extending from the common iliac to the common femoral artery. The inguinal canal was reconstructed using the fibrous tissue which had surrounded the graft. The operation relieved the symptoms and the patient returned to his work.

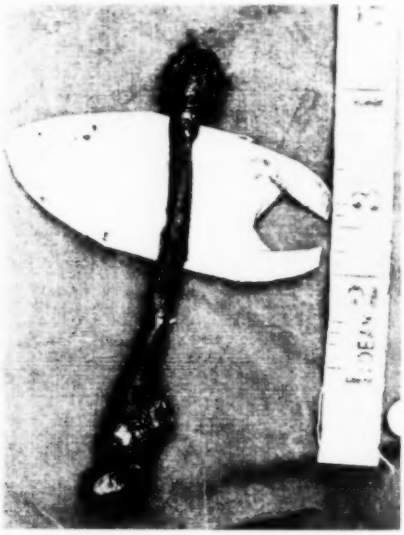

FIG. 473.—Operative specimen of obstructed right external iliac artery with associated inlay plastic graft used in the repair of inguinal hernia.

Comment.—Patients who have had an inlay used for the repair of an inguinal hernia have complained of discomfort in the groin when stooping (Thompson, 1948), but no reference has been found in the literature to thrombus formation in an artery due to pressure of a rigid inlay used in the repair of an inguinal hernia.

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TORSION OF FATTY TAG IN FALCIFORM LIGAMENT SIMULATING PERFORATED PEPTIC ULCER

By A. W. BEASLEY

LATE SURGICAL REGISTRAR, ST. MARGARET'S HOSPITAL, EPPING

WHILE the presence of quantities of fat in the substance of the falciform ligament is a common finding, this fat is usually incorporated evenly so that the ligament presents a smooth surface.

That such fat should project as a pedunculated mass from the surface is less common, and that such a tag should undergo torsion and thereby present as an abdominal emergency is a condition which does not appear to have been recorded in the literature.

In the following case the symptoms resembled those of a perforation of a peptic ulcer.

CASE REPORT

The patient, a woman aged 53, was referred for admission by her general practitioner on Aug. 31, 1956. She had a history of recurrent lumbar backache, and was convalescing from an attack for which she had been confined to bed for the first half of August, and of attacks of right-sided abdominal pain, related to fatty meals, relieved by vomiting, and unaccompanied by jaundice.

Two days before admission she developed colicky pain across the mid-abdomen, which subsequently passed up to the right hypochondrium after the usual fashion. On the afternoon of admission, however, it became suddenly severe with some change of character; while still colicky, there was a background of continuous pain, increased with inspiration and immediately on taking food or drink. Her admission note described "a little resistance over the right upper quadrant, with moderate tenderness over the gall bladder region".

On admission her temperature was 97·2° F. (36·2° C.), pulse 66, blood-pressure 135/75. The abdomen was soft, apart from some guarding of the right rectus; there was general tenderness on the right side. Jaundice was absent. Laboratory investigations on admission showed no abnormality of blood or urine.

The following day, Sept. 1, 1956, her pain was still severe. She was anorexic and slightly dehydrated. Her temperature and pulse remained subnormal (98° F. (36·6° C.), pulse 64); her blood-pressure had fallen to 100/60 and she was pale and apprehensive. Her abdomen now showed marked guarding and rigidity in the right hypochondrium, with rebound tenderness. Plain radiographs of the abdomen showed no air under the diaphragm, but a rather diamond-shaped shadow which could be taken to outline the right compartment of the lesser sac.

Although her recent severe pain was now of twenty-four hours' duration, and there was still no pyrexia, her marked peritonism was sufficiently suggestive of perforation of an acute peptic ulcer (possibly into the lesser sac) to call for laparotomy. This was undertaken under general anæsthesia on the evening of Sept. 1, 1956.

On the right side of the falciform ligament, close to its free border, was a flat leaf-like tag of fatty tissue which had undergone torsion through four turns and was purple and congested (*Fig.* 474). The base was ligated and the tag excised. The other viscera were normal. The abdomen was closed in layers without drainage.

The patient was free of her pain when she recovered from the anæsthesia, and her convalescence was uninterrupted.

Histological report on the specimen was: "An oval piece of fatty tissue 1·5 × 1·0 cm., and 0·5 cm. thick, with a twisted tag of pedicle attached to a point on its edge. It is reddish purple in colour. Histologically it has a lipomatous structure with intense vascular engorgement and fairly extensive interstitial hæmorrhages."

FIG. 474.—Specimen before fixing. (*Natural size.*)

This woman presented with a past history of lumbar and abdominal pain, and with an acute episode which had to be differentiated from her previous condition. It then came to resemble the clinical picture of a perforated acute peptic ulcer, with the distinction that after twenty-four hours of acute pain the temperature and pulse remained subnormal. The exacerbation of pain which accompanied the taking of food or drink, and which was regarded as supporting the diagnosis of perforation, can perhaps be best explained as due to pressure on the twisted tag with peristaltic activity of the stomach.

SUMMARY

1. A case of torsion of a tag on the falciform ligament, lipomatous in character, is described.

2. The symptoms resembled those of perforation of a peptic ulcer, in the differential diagnosis of which no previous record of this present condition has been found.

Acknowledgements.—I am grateful to Mr. H. W. S. Wright for permission to record this case, and to Dr. I. M. Tuck for her report on the specimen.

REVIEWS AND NOTICES OF BOOKS

The British Encyclopædia of Medical Practice. Medical Progress 1958. Editor-in-Chief, THE LORD COHEN OF BIRKENHEAD, M.D., D.Sc., LL.D., F.R.C.P., Professor of Medicine, University of Liverpool. $9\frac{3}{4} \times 6\frac{1}{2}$ in. Pp. 341+vii. 1958. London: Butterworth & Co. (Publishers) Ltd. 37s. 6d.

THE present large volume is made up of three parts: the first is devoted to fifteen excellent critical reviews; the second to drugs; while the third part deals with abstracts from 'accessory nasal sinuses' to 'vitamins'.

The critical reviews form a fine collection of articles dealing with medicine, surgery, obstetrics and gynæcology, anæsthesia, and many other subjects.

Professor Stammers is responsible for the critical review on surgery and he has completed his task with distinction and he emphasizes the hazards to which disturbances of fluid balance and corticosteroid therapy expose the surgical patient.

The outstanding critical review comes from the pen of Sir Ernest Rock Carling, who writes on radiation hazards. This is a masterly account and should be read by all doctors. No topic has given rise to more discussion in recent years than the hazards of the various forms of radiation. The ever-increasing number of cases of leukæmia in early life should be a warning of the dangers of X rays to the pelvis of pregnant mothers.

This *Medical Progress 1958* is a book which should be available for reference to all doctors.

Year Book of Cancer, 1957–1958. Edited by RANDOLPH LEE CLARK, jun., B.S., M.D., M.Sc. (Surgery), D.Sc. (Hon.), Director and Surgeon in Chief, The University of Texas; and RUSSELL W. CUMLEY, B.A., M.A., Ph.D., Director of Publications, The University of Texas. $7\frac{1}{2} \times 5$ in. Pp. 523, with 191 illustrations. 1958. Chicago, Ill.: The Year Book Publishers Inc. (London: Interscience Publishers Ltd.) 60s.

THIS latest addition to the 'Year Book' series seeks to give an account of the important papers on cancer published during the preceding year. The very wide scope covered is indicated by the fact that an editorial board of 124 members selected 235 articles from a total of approximately 4000 published during the course of the year, but of this number of articles selected only 53 appeared in foreign journals and of these 37 were in English. The editors claim, however, that English being 'the language of science', all important advances, even those first seeing the light of day in foreign journals, would sooner rather than later find expression in the English language. The book is planned mainly on a regional basis and these articles are predominantly of surgical interest. Nevertheless, Epidemiology, Biochemistry, Physics, Radiobiology, Genetics, and Virology are dealt with, but somewhat perfunctorily. This arrangement leads to a somewhat piecemeal approach and little guidance is given to the reader in the way of selection, articles propounding opposite points of view often being placed in juxtaposition. Advances in the surgery of cancer are unlikely to lead us very far, and it is a pity that more space has not been devoted to the basic disciplines which hold out more hope for advance and which are at present in the forefront of the battle.

Lest the preponderance of articles in English should lead the reader to suspect a parochial approach, the chapter on 'Oncology in the Soviet Union' by Michael Shimkin should dispel this view. The final paragraph in this chapter is worthy of quotation: "In cancer research, as in other aspects of medical investigations, we were impressed by the thorough and intimate knowledge of the American and British work displayed by the Soviet scientists. We were also dismayed by our own ignorance of the work and accomplishments of our Soviet colleagues. It is our impression and conclusion that the Soviet Union has many talented, original scientists, working in laboratories that are adequately equipped, and that their contributions deserve and require our thoughtful attention and evaluation."

This book can be recommended as a useful work of reference for the surgeon practising cancer surgery.

Treatment of Breast Tumors. By ROBERT S. POLLACK, M.D., F.A.C.S., Clinical Instructor in Surgery, Stanford School of Medicine; Clinical Instructor in Surgery (Oncology), University of California School of Medicine. $10 \times 6\frac{3}{4}$ in. Pp. 147, with 47 plates and 16 text figures. 1958. London: Henry Kimpton. 45s.

THIS monograph represents the treatment of breast tumours as carried out by Dr. Robert Pollack and his medical colleagues of the University of California School of Medicine. There are certain differences in ideas as contrasted with the British School.

We do not believe that there is any connexion between the apical axillary nodes and those in the supraclavicular area. There is only one way in which the supraclavicular nodes can become involved and that is via the mediastinal lymphatics to be found lying along the internal mammary vessels. Although the extended radical mastectomy is advocated in some parts of Amercia it is rarely practised in England. If the internal mammary lymphatics are invaded with cancer, high-voltage X rays give better results than surgical excision.

This monograph is well illustrated and the plates are well produced. There are several blank pages in this monograph which the printer's ink has missed altogether.

Tumors and Tumorous Conditions of the Bones and Joints. By HENRY L. JAFFE, M.D., Director of Laboratories and Pathologist, Hospital for Joint Diseases, New York. 10×7 in. Pp. 629, with 701 illustrations as 194 figures. 1958. London: Henry Kimpton. 135s.

THIS is a very comprehensive atlas dealing with bone tumours together with a most extensive radiographic and pathological series of illustrations, all of which are of high quality and beautifully reproduced. The photo-micrographs are particularly fine.

All the common and rare tumours of bone are carefully described and illustrated. Adamantinoma of the limb bones is the best illustrated description of this rare tumour that we have so far seen.

This work will prove invaluable to physicians, surgeons, radiologists, and pathologists as a reference volume. It is by far the best work which has been published.

Cancer. Edited by RONALD W. RAVEN, O.B.E. (Mil.), T.D., F.R.C.S., Joint Lecturer in Surgery, Westminster Medical School, University of London. Volume 4, Part VIII, Clinical Aspects. $9\frac{1}{2} \times 6\frac{1}{2}$ in. Pp. 532 + xii, fully indexed, with 173 illustrations. 1958. London: Butterworth & Co. (Publishers) Ltd. 85s.

VOLUME 4 of this now famous work covers the clinical aspects of cancer. As before, a distinguished team of contributors has been assembled and the editor has

himself written the chapters on the Lips and Mouth, the Pharynx, the Œsophagus, and the Breast. Michael Harmer opens the batting with an excellent article on the TNM system of staging cancer which is now in the process of being adopted internationally and will undoubtedly supersede all other systems. Inevitably the present volume bears more resemblance to a student's text-book than those which have gone before, and it is doubtful how far a recitation of classical physical signs will be of much value to the likely readers of this work who will, for the most part, be expert in their fields.

However, this excellently written and beautifully produced volume nicely rounds off the more exciting disquisitions in the earlier volumes and without it the carping critic would undoubtedly have complained that the most valuable part of our knowledge as it affects the patient to-day would have been left out.

When so much is excellent it might be invidious to select any particular article for mention, but the chapter on the Thyroid by Victor Riddell is a model of concise and clear presentation. His comments on frozen-section examination are nevertheless somewhat conflicting, and the difficulties of interpretation of thyroid histology are so notorious (as he remarks) that many surgeons would prefer to subscribe to his final injunction that "In many instances it will be wiser to allow the extra time necessary for an examination of multiple paraffin blocks", indeed they might prefer the word 'all' to 'many'.

The collaboration of a much admired transatlantic colleague in the person of George Pack has been secured in the chapter on Sarcoma of Soft Tissues written by him and Irving Ariel. No doubt the English surgeon who has had more experience of these lesions than perhaps anyone else in the world was too busily engaged to be included in the team, but it would have been nice to see a reference to his work at the end of this chapter.

In the chapter on Bone Tumours it is stated that "Trabeculation is not a striking feature of a giant-cell tumour", yet the two radiographs illustrating this disease show trabeculation and this feature would be regarded as an important point of differential diagnosis by most clinicians.

Undoubtedly a work of such range must contain statements with which any individual reviewer would be in disagreement. Taken as a whole, however, this work maintains the superb standard of the previous volumes and is an elegant and welcome addition to the surgeon's library.

Comparative Anatomy and Physiology of the Nose and Paranasal Sinuses. By Sir VICTOR NEGUS, Hon. D.Sc. (Manch.), M.S. (Lond.), F.R.C.S. (Eng.), Consulting Surgeon to the Ear, Nose, and Throat Department, King's College Hospital. $9\frac{3}{4} \times 6\frac{1}{4}$ in. Pp. 402 + xv, with 178 illustrations. 1958. Edinburgh and London: E. & S. Livingstone Ltd. 70s.

IN this, his latest book, Sir Victor Negus has given to the reader the benefit of many years of patient research into the comparative anatomy and physiology of the nose and the result is not only pleasing to read in its entirety but also serves as a most valuable work of reference by reason of its excellent comprehensive index and by the impressive list of no less than 317 other publications on the same or related subjects. But this is no mere recapitulation of the investigations and conclusions of other workers; its outstanding feature is the reasoned and critical presentation of deductions from the writer's own observations and experiments. The information is easy of assimilation, the excellent illustrations, many of which refer to specimens prepared and presented to the museum of the Royal College of Surgeons by the author, serving to elucidate the complexities of form and function found in this region.

The first, and by far the longest, of the three parts into which the book is divided is concerned with the comparative anatomy, both macroscopical and microscopical, and the physiology of the nose together with a study of the action and minute structure of cilia, knowledge of which has been increased by recent investigations by means of the electron microscope. The paranasal sinuses are dealt with in a similar way in the second part, while the third relates exclusively to the human nose and accessory sinuses. In the summary to this last part the author points out that "while the nose of many vertebrates has reached a high degree of perfection for humidification, for olfaction, or for rapid transference of air currents adequate for efficient respiration, the organ in Man is a rather poor affair, with a small surface for the warming and moistening of air and with an attenuated olfactory area".

To conclude, this is a work of immense value, not only to the human and comparative anatomist but to the medical specialist; the anthropologist, too, will find much to interest him in the Appendix dealing with the evolutionary history of Man from the evidence of the nose and larynx.

This is yet another example of a fine production from the publishers, Messrs. E. & S. Livingstone Ltd.

Medicine and the Navy, 1200–1900. By J. J. KEEVIL. Vol. II, 1649–1714. $8\frac{3}{4} \times 6\frac{3}{4}$ in. Pp. 332 + xii, with 18 plates. 1958. Edinburgh and London: E. & S. Livingstone Ltd. 40s.

THIS second volume of the medical history of the Navy by the late Dr. Keevil begins with an account of affairs at the end of the Civil War, followed by a review of the enactments made during the Commonwealth and Protectorate period relating to the care of sick and wounded naval personnel. That this was a most progressive and constructive period is not generally realized. Charles II was, in fact, able to take over the nucleus of a strong and efficient naval force which included 154 warships, two of which, the *Warspite* and the *Defiance*, were so designed that stores for six months, instead of the ten weeks previously considered practicable, could be accommodated, a great advantage especially during wartime when the need for frequent restocking presented a major problem.

The two famous diarists of the seventeenth century, John Evelyn and Samuel Pepys, played important parts in the reconstruction of the Navy and the amelioration of its medical services during the later Stuart period. The able and energetic Pepys did much to eradicate abuses in the general organization. Evelyn's task was especially difficult. He had been appointed in 1664 one of the Commissioners for the Sick and Wounded and Prisoners during the Dutch Wars and indeed continued to perform his duties when the other members neglected them through fear of the plague. During the sixty-five years reviewed in this volume this country was involved in no less than six wars and the unpopularity of naval service presented a medical as well as a national problem, for it was only too well known that casualties from the dreaded scurvy were more numerous than those resulting from enemy action. Although it had long been realized that the presence of a surgeon or even a surgeon's mate on board was of inestimable benefit, nevertheless, in times of national emergency all medical services tended to be radically reduced on the grounds of economy.

Like the first volume of this great work, this new section presents a complete and fascinating story that will appeal to all readers, but especially to those whose interests are medical, naval, or historical. It is a picture of English history taken from the particular view of the naval medical service, and those who may desire to study any particular period more fully are provided with ample references for further reading. Once again the publishers,

Messrs. E. & S. Livingstone Ltd., are to be congratulated on the excellence of their production.

British Obstetric and Gynæcological Practice. Edited by Sir EARDLEY HOLLAND, M.D. (Lond.), F.R.C.P., F.R.C.S., F.R.C.O.G., Consulting Obstetric and Gynæcological Surgeon, London Hospital; and ALECK BOURNE, M.A., M.B., B.Ch. (Cantab.), F.R.C.S., F.R.C.O.G., Consulting Gynæcologist, St. Mary's Hospital, London. Second edition. 9¼ × 7 in. Pp. 891 + xii, fully illustrated. 1958. London: William Heinemann Medical Books Ltd. 105s.

THE second edition of this important work has been very thoroughly revised by the large team of contributors.

There can be little doubt that this volume, devoted as it is to every phase of gynæcology, is completely representative of the methods and techniques adopted by British gynæcologists both at home and abroad. The whole book is beautifully illustrated with clinical, radiological, and pathological pictures, some of which are in colour.

Professor T. N. A. Jeffcoate has written an excellent chapter on 'Disorders of Menstruation' which is very comprehensive and complete.

Endometriosis, a subject which interests the general surgeon because of its possible distribution in many abdominal organs, has been covered by Mr. John Howkins, who has revised this chapter in a masterly way.

This work is a great credit to British gynæcologists and to the publishers.

Clinical Radiology of Acute Abdominal Disorders. By BERNARD S. EPSTEIN, M.D., Chief, Department of Radiology, The Long Island Jewish Hospital, New York. 10 × 6¾ in. Pp. 352, with 406 illustrations on 224 figures. 1958. London: Henry Kimpton. 112s. 6d.

DURING the last decade the abdominal surgeon has received more and more help from his radiological colleague in the diagnosis of acute abdominal conditions. This book deals with the various clinical conditions in which the radiologist can be of help to the surgeon. Of necessity the book requires to be amply illustrated and this the author has done, for there are more illustrations than pages in the book.

The numerous radiographs are good and well reproduced and they reveal both common and rare congenital and acquired acute abdominal conditions.

The book is divided into four large chapters: the first deals with congenital disorders; the second with neoplastic diseases; the third with inflammatory, parasitic, and vascular disorders; while the fourth is devoted to traumatic disorders, foreign bodies, and the effects of drugs. There is an excellent index of authors as well as a subject index, but British authors or their works are hardly mentioned.

Surgery of the Sympathetic Nervous System. By Sir JAMES PATERSON ROSS, K.C.V.O., LL.D., M.S., F.R.C.S., F.R.A.C.S., F.A.C.S., Director of the Surgical Professorial Unit, St. Bartholomew's Hospital, London. Third edition. 9 × 6 in. Pp. 170 + xii, with 51 illustrations. 1958. London: Baillière, Tindall & Cox Ltd. 35s.

THE third edition of this book is published at an opportune time, for it is some twenty-five years ago that the first edition appeared, and in that intervening period of a quarter of a century much has happened in the surgery of the sympathetic nervous system and a complete reassessment was necessary.

This reassessment has necessitated the complete rewriting of the book. Now we have the latest word on surgery of the sympathetic nervous system as practised by British surgeons. We are delighted with the forthright yet lucid style the author has adopted. The illustrations, though few, are well chosen and clear and do enhance the value of the text. There can be little doubt that this book will appeal not only to general surgeons but also to orthopædic and neurosurgeons, and to anatomists as well.

The price of the book is very moderate for a modern medical monograph.

Head Injuries. By E. S. GURDJIAN, M.D., Professor of Neurological Surgery, Wayne State University College of Medicine; and J. E. WEBSTER, M.D., Associate Professor of Neurological Surgery, Wayne State University College of Medicine. 9¼ × 6 in. Pp. 482, with 108 illustrations. 1958. London: J. & A. Churchill Ltd. 100s.

THIS book deals with the mechanisms, diagnosis, and management of head injuries and reflects the experience of the authors over a twenty-five year period. It also considers the data derived from 1285 cases of head injury treated at the Detroit Receiving Hospital between January, 1952, and July, 1954, and from 151 consecutively autopsied cases of head injury.

With this large clinical survey the authors have produced a very comprehensive and eminently practical monograph. The wealth of clinical and post-mortem material has allowed the authors plenty of scope with regard to illustrations.

Every aspect of head injury has been well covered and the various forms of operative treatment are well described.

In this mechanical age, in spite of every warning, head injuries are on the increase in most countries, and therefore there is ample room for a book of this calibre which deals with head injuries in a very full and comprehensive manner.

An Atlas of Surgery. By F. WILSON HARLOW, M.B., B.S. (Durham), F.R.C.S., Fellow of the International College of Surgeons; with a Foreword by Sir CECIL WAKELEY, Bt., K.B.E., C.B., LL.D., D.Sc., F.R.C.S. 13¼ × 8¼ in. Pp. 363 + xiv, with 1292 illustrations. 1958. London: William Heinemann Medical Books Ltd. 50s.

HERE is a picture book (there are nearly 1300 illustrations) which should be popular with all students of surgery, for, as Sir Cecil Wakeley says in his preface, "there can be no doubt whatever that a good picture is worth innumerable pages of the written word". Many of us would share his wish that such a book had been available when we were students! What a relief it would have been to the much reading of text-books. There are eight sections dealing respectively with abdominal surgery, urology, gynæcology, general surgery, special surgery which includes, ear, nose, and throat, thoracic and neurosurgery, orthopædics, the management of operations, and surgical pathology. Although a list of text-books to which reference has been made is given, the source of some of the illustrations is not indicated nor are the names of the authors from whose papers they have been taken. A bald reference, "from the *British Medical Journal*", without year or page is not very helpful. This is a defect which could with advantage be remedied in a future edition so that the student would know where to extend his inquiries if he so desired. The addition of an index would also be an advantage. It is realized, however, that the book is an atlas or chart and needs to be accompanied with appropriate sailing directions in the form of text-books, to which it is both an instructive and accurate guide. The illustrations are clear, the text brief and to the point and easily readable, and the whole atlas is so

attractive that it should have a wide appeal. It very well fulfils the author's object of providing a pictorial *aide-mémoire* of common and important surgical facts and procedures, and countless medical students should be grateful for this aid to learning surgery.

Electrolyte Changes in Surgery. By KATHLEEN E. ROBERTS, M.D., Assistant Chief of Medicine, United States Public Health Service Hospital; PARKER VANAMEE, M.D., Assistant Physician, Memorial Hospital for Cancer and Allied Diseases; and J. WILLIAM POPPELL, M.D., Chief, Section of Cardiopulmonary Physiology and Associate, Sloan-Kettering Institute for Cancer Research, New York. 8½ × 5 in. Pp. 113 + x, with 20 illustrations. 1958. Springfield, Illinois: Charles C. Thomas. (Oxford: Blackwell Scientific Publications.) 34s.

CERTAIN problems of electrolyte balance which are peculiar to surgical patients, especially in connexion with operative procedures, are discussed with particular reference to abdominal and thoracic surgery. It is pointed out that operations which do not involve the body cavities present fewer problems of electrolyte imbalance.

The flyleaf description of the book as a primer for the clinician is accurate and the pathogenesis and correction of the electrolyte changes occurring in renal disease, hepatic insufficiency, and extensive gastro-intestinal operations are well discussed. Its five chapters deal respectively with the pre-operative period, the post-operative changes in water and electrolytes, alteration in the acid-base balance, complications of gastric and intestinal resection, including the physiology of the 'dumping syndrome', hepatic failure, and renal disease. Two appendices, one entitled 'Philosophy in the Diagnosis and Treatment of Electrolyte and Water Problems' and a second consisting of a table of conversion factors, and finally some 36 references complete the text. There is no index. This is well printed in clear, dark type and the small volume has a pleasing appearance. It is interesting to note that one of the conclusions of the authors is that "the most common electrolyte abnormality encountered in clinical medicine is a 'laboratory error'", and most surgeons will support their plea for a healthy scepticism where the clinical impressions and sequence of events are not confirmed by laboratory data.

Modern Trends in Surgical Materials. Edited by LEON GILLIS, M.B.E., M.Ch. (Orth.), F.R.C.S. (Eng.), F.R.C.S. (Edin.), D.L.O., Consultant Surgeon, Queen Mary's (Roehampton) Hospital, East Ham Memorial Hospital, and St. John's Hospital, London. 9½ × 6½ in. Pp. 266 + xii, with 96 illustrations. 1958. London: Butterworth & Co. (Publishers) Ltd. 72s. 6d.

A BOOK on the materials used by surgeons is welcome, especially when the sections of which it is composed are written by those who are leaders in the particular branches of surgery on which they write, and under the general editorship of Mr. Leon Gillis, whose work at Roehampton is so well known. Paraphrasing a well-known remark of Sir Winston's, he writes: "Give us the right tools and we will make a better job of what we are doing". How true this is when applied to materials! It is half the battle to have the best of these for the particular purpose for which they are required, and how true also is his observation that the ideal implant is that which is absorbed by the body, a condition which only a graft can fulfil. Some idea of the scope of the book can be gathered from such chapter headings as, The Metallurgical Problems in Surgery, Plastics, Biomechanics, Preservation of Tissues, and Sterilization. There are articles from abdominal, plastic, orthopædic, vascular, and dental surgeons, while there is also a chapter on anæsthetics. In all there are twenty-two chapters. An important and interesting section deals with fascial and dural substitutes and absorbable hæmostatic agents which include such materials as fibrin foam, fibrin and gelatin film, and gelatin sponge, most of which are being increasingly used by surgeons. The history of these materials is interesting and a future edition might perhaps contain a brief account of their development, from the time of Horsley's use of human muscle and de Martel's of the pectoralis of the recently killed pigeon. The book is well printed and illustrated and the apt quotations from William Penn and Robert Hutchison which begin and end it add to its attraction. A bibliography and references are given after most of the chapters and it is well indexed, and most progressive surgeons will want to have it on their bookshelves.

Ptoses Abdominales et Prolapsus Pelviens. By LUCIEN DIAMANT-BERGER. 9½ × 6 in. Pp. 194, with 119 illustrations. 1958. Paris: Doin.

THIS short monograph deals with ptosis and prolapse of the abdominal and pelvic viscera—a group of conditions characterized by poor supporting tissues and muscles. The syndrome as it affects each organ is described, with details of surgical treatment. The various 'pexies' for stomach, liver, colon, and kidney have long ago disappeared from English text-books on operative surgery, and the operations for rectal prolapse include neither anterior resection nor Roscoe Graham's operation.

The conventional operations for genital prolapse are described and also a sling procedure for post-hysterectomy vaginal prolapse.

No references are given, the author stating that the text represents "the opinions of a man who has read, reflected, and operated a great deal" on this subject. The majority of views expressed are, however, unlikely to meet with the approval of the reader in this country.

Cold Injury, Ground Type. By TOM F. WHAYNE, M.C., U.S.A. (Ret.), Professor of Preventive Medicine, School of Medicine, University of Pennsylvania; and MICHAEL E. DEBAKEY, M.D., Professor of Surgery and Chairman of the Department, Baylor University College of Medicine, Houston, Texas. 9¾ × 6½ in. Pp. 570 + xxii, with 105 illustrations. 1958. Washington, D.C.: Office of the Surgeon General, Department of the Army. $6.25.

THIS handsome large monograph contains a wealth of information gained in the various fields of hostilities in World War II by the medical personnel of the United States Army. The volume is profusely illustrated and there are many excellent coloured plates.

Every facet of frost-bite, trench-foot, immersion foot, and gangrene is dealt with in a most comprehensive manner.

It is interesting to note that the Medical Corps of the United States Army were convinced that losses occurred because lessons of the past were not learned. The British experience in World War I was not recollected by the United States in World War II. The experience of the Aleutians was not transferred to the Mediterranean Theatre. The experience of that theatre was not transferred to the European Theatre. It is significant to learn that the total number of cold injury cases in all theatres for the entire war was 91,000.

The editors point out that cold and wet, either singly or in combination, are the basic causes of cold injury. Predisposing factors were also of great importance in World War II. These factors included the intensity of

combat; the inadequacy of clothing and footgear, and the pressure of events which required that new troops be taught so much in a limited period of time that they were not taught the essential facts of cold injury.

General Omar Bradley himself has acknowledged the fact that a calculated risk was taken, for which a price had to be paid, when in the summer and early autumn of 1944 it was decided that petrol and ammunition should take precedence in transportation over supplies of winter clothing.

Let us hope that if there is ever another World War the lessons of the former conflicts will be remembered.

It is to be hoped that every medical library will contain a copy of this work, for as a work of reference it could not be surpassed.

Notes de Techniques Chirurgicales de 'La Presse Médicale'. Collected by LUCIEN LEGER. 9½ × 6½ in. Pp. 313+viii, with 209 illustrations. 1958. Paris: Masson et Cie. 3800 fr.

THIS is a collection of short articles that have appeared in *La Presse Médicale* during the past ten years. Where necessary they have been re-edited and are arranged in sections covering the various branches of surgery, including gynæcology and orthopædic surgery. Many of the articles are so short and describe such well-established procedures that their inclusion is surprising. Such notes are those on omental plugs for closure of perforated ulcers and the closure of colostomies. There are the usual 'new' hernia operations together with several complicated operations for various conditions that are certainly better dealt with by simpler methods.

However, the articles by such authorities as L. Leger, J. and R. Judet, L. Barraya, A. Brunschwig, and others make absorbing reading. It certainly illustrates the present interests of many French surgeons.

Frontiers of Healing. By GEOFFREY MURRAY. Pp. 256. 1958. London: Max Parrish. 16s.

THE author has marshalled his facts well in this book and puts forward a plea that treatment by so-called 'quacks' should be given a more thorough trial than in the past.

His story of Sir Herbert Barker, so-called founder of manipulative treatment, makes interesting reading.

One is not impressed with the stories and miracles of Lourdes, but others may be more convinced as to their significance.

Geoffrey Murray has much to say on the problem of cancer and he is quite *au fait* with the organizations which collect money in order that one day a cure may be found.

The book makes interesting reading because quite a number of its pages are devoted to medical history. The author considers that medicine was made for man, not man for medicine.

Emergency Surgery. By HAMILTON BAILEY, F.R.C.S. (Eng.), F.A.C.S., F.R.S.E., Emeritus Surgeon, Royal Northern Hospital, London; Consulting Surgeon, The Italian Hospital; General Surgeon, Metropolitan Ear, Nose, and Throat Hospital. Seventh edition. 9¾ × 6½ in. Pp. 1197 + xvi, with 1576 illustrations. 1958. Bristol: John Wright & Sons Ltd. 189s.

THIS is the seventh edition of this well-known work and it is certainly the best, and Mr. Hamilton Bailey is to be congratulated on what we consider his masterpiece. This new edition is superbly illustrated with some 1576 illustrations, many of which are colour. The author is certainly a past master in the field of medical illustration.

Emergency surgery is still as important as ever, and the younger generation of surgeons will find this book a valuable help in time of trouble. When to operate, when not to operate, and how to operate under emergency conditions is the theme of this work.

An interesting page of photographs depicting Mr. Bailey's teachers at the London Hospital and elsewhere is to be found at the front of this volume. The names certainly are those who have added lustre to British surgery in the past.

We are pleased to read that this book is supplied to all sea-going ships of Her Majesty's Navy. The Senior Service is well provided for in any emergency.

We have nothing but praise for this book; it is a real credit to British surgery.

The Esophagus. Medical and Surgical Management. By EDWARD D. BENEDICT, M.D., F.A.C.S., Assistant Clinical Professor of Surgery, Harvard Medical School; and GEORGE L. NARDI, M.D., F.A.C.S., Clinical Associate in Surgery, Harvard Medical School. 9¾ × 6½ in. Pp. 390, with 108 illustrations. 1958. London: J. & A. Churchill Ltd. 105s.

THIS comprehensive large monograph deals with all aspects of diseases of the œsophagus. Since the second world war the surgery of the œsophagus may be said to have come into its own. The thoraco-abdominal approach has revolutionized the treatment of cancer of the œsophagus. The book is well illustrated and contains some sixteen coloured plates which have been beautifully reproduced.

The various surgical techniques are clearly explained and the reproduction of the many and varied radiographs is good.

This monograph gives an excellent account of the American treatment of tumours and conditions of the œsophagus.

Professor Edward D. Churchill writes a foreword to the book.

A Text-book of Surgery. By PATRICK KIELY, B.Sc., M.D., M.Ch. (N.U.I.), F.R.C.S. (Eng.), Professor of Surgery, University College, Cork; Examiner in Surgery, National University of Ireland. Second edition. 9¾ × 6 in. Pp. 1158 + x, with 610 illustrations and 22 coloured plates. 1958. London: H. K. Lewis & Co. Ltd. 63s.

THIS text-book now appears in a second edition; it is a comprehensive 'one author' book and has the advantage that it is cheap and so the student can purchase it. Its great drawback is in its illustrations. Although there are some 605 of them, yet the majority are poorly produced, some have been copied and modified from other text-books, and quite a number do not really represent the clinical condition in the legend. For instance Fig. 216 is upside down, Fig. 515 is a poor drawing of a hard chancre, and Fig. 508 is not like a cyst of the epididymis.

The student of to-day does not require to be familiar with Young's radical operation for tuberculosis of the male genital tract, nor is it necessary to illustrate this operation.

However, having been critical of the illustrations, the book itself covers the whole field of surgery, including the surgery of the eye, ear, nose, and throat in a very competent fashion.

Surgeon at Arms. By DANIEL PAUL and JOHN ST. JOHN. 7¾ × 5 in. Pp. 227, with 15 plates. 1958. London: William Heinemann. 16s.

THIS is the war history of Daniel Paul, a surgeon from South Africa who served in the First Airborne Division. After a short course of training in England he was dropped by parachute at Arnhem in September, 1944. He worked

in a Dutch hospital which was soon taken over by the Germans. His account of the various casualties and the long operation lists is interesting and provides another facet in the medical history of World War II. Not many weeks later Paul finds himself in a prisoner-of-war camp which he detests and soon makes his escape with three others. He gives an interesting and revealing description of the various Dutch underground agents and the great risks they took to get the British soldiers through the German lines back to their own units.

The outstanding feature of this book is the tenacious opposition of the ordinary Dutch people to the German occupation. The Dutch people themselves paid heavily for helping the British and American soldiers; in one instance the Grune Polizer fell on the village of Putten and seized all the men and took them away to be shot, while the women and children were locked in the church—and, after an orgy of looting, all the houses were set alight.

An interesting account of how many escapes were planned and executed during the last war.

Milestones in Modern Surgery. By ALFRED HURWITZ, M.D., Professor of Surgery, State University of New York College of Medicine, New York City; and GEORGE A. DEGENSHEIN, M.D., Assistant Attending Surgeon, Maimonides Hospital. 9¼ × 6 in. Pp. 520 + xviii, fully illustrated. 1958. London: Cassell & Co. £5 12s. 6d.

WE are living in an age when the medical profession as a whole is interested in the history of the past and, therefore, this volume is opportune. For the most part we agree with the arrangement of the book and the medical men singled out because of the impact they have made by their discoveries over the years.

However, the book is overweighted with the names of American pioneers; only four names come from the British Isles, namely, Spencer Wells, Fleming, Ernest Miles, and Souttar; one would have thought that Lister, Macewen, Victor Horsley, and Robert Jones had earned a place in the history of *Milestones in Modern Surgery*, for what they did to alter the surgical treatment of disease.

The book is well presented, but what a pity the illustrations are so poor; surely better pictures of the famous men recorded in this volume could have been obtained.

Atlas of Technics in Surgery. By JOHN L. MADDEN, M.D., F.A.C.S., Director of Surgery, St. Clare's Hospital; Associate Clinical Professor of Surgery, New York Medical College; with 62 contributors. 11¾ × 9 in. Pp. 648 + xx, with 293 full plates. 1958. New York: Appleton-Century-Crofts Inc. (London: Mayflower Publishing Co.) Approx. £14.

THIS very large volume depicting surgical technique has been written primarily for the surgeon in training and it certainly does give the reader the standard operative procedures of American surgeons. As there are some sixty-two contributing authors from various parts of the United States, the book may be looked upon as authoritative.

The various stages of the standard operations are beautifully drawn and reproduced. There can be little doubt that good drawings of operative details are far better than photographs as the medical artist is able to stress the points which the surgeon wishes to emphasize.

It is true that British and American surgeons may differ in operative technique and details, but there is very considerable agreement in the majority of operations.

This book will take its place as one of the really useful books which every surgeon should possess. The only criticism which can be levelled against the book is its enormous size and weight; in the next edition we hope the publishers will insist on two volumes to replace this single cumbersome one.

Peripheral Nerve Injuries. By RUTH E. M. BOWDEN, D.Sc., M.B., B.S., L.R.C.P., M.R.C.S., Professor of Anatomy, Royal Free Hospital School of Medicine, University of London. 7¼ × 4⅝ in. Pp. 62 + viii, with 30 illustrations. 1958. London: H. K. Lewis & Co. Ltd. 8s. 6d.

THE author, who during the second world war was a member of the team of the Nerve Injuries Unit at Oxford, tells us that her object has been to introduce the methods of diagnosis and treatment of nerve injuries to physiotherapists, medical students, and house officers and to produce an *aide-mémoire* to their seniors. Professor Seddon remarks in a foreword that almost all of the best work on nerve injuries, from the time of Weir Mitchell onwards, has been done in time of war, but the sporadic incidence of these lesions in peacetime creates the need for a small handbook such as this. His commendation will do much to popularize the book which well achieves the author's object, but it must be realized that parts of it are bare outlines and the useful suggestions for further reading on page 58 need to be followed to fill in or expand these outlines so that wrong impressions may not be made. As a guide to principles the little book can be warmly recommended.

Emergency War Surgery. N.A.T.O. Handbook. Prepared for use by the Medical Services of N.A.T.O. Nations. 7¾ × 5 in. Pp. 411 + xii. 1958. Washington, D.C.: United States Government Printing Office. $2.25.

THIS monograph should prove of real value to both civilian and military surgeons; it is in itself a combined operation, for it was developed by a committee of three surgical consultants representing the military medical services of France, the United Kingdom, and the United States. Material has also been gleaned from authors and publications of many NATO countries.

There can be little doubt that in spite of its compactness (it was designed to fit the pocket of the field uniform) and its conciseness, this is an extremely practical book. It covers the care of casualties in forward areas, from the battlefield to field and evacuation hospitals. The actual surgical procedures are described in a lucid way and the book can be looked upon as an excellent treatise on traumatic surgery. An excellent production, and the book can be recommended not only to resident medical officers but also to registrars and surgeons alike.

A Method of Anatomy. By J. C. BOILEAU GRANT, M.C., M.B., Ch.B., F.R.C.S. (Edin.), Professor Emeritus of Anatomy, University of Toronto. Sixth edition. 9⅞ × 6⅞ in. Pp. 879 + xxvi, with 862 illustrations. 1958. London: Baillière, Tindall & Cox Ltd. 88s.

THE usefulness and popularity of this work can be judged by the fact that six separate editions have appeared in just over twenty years.

Although there are many anatomical text-books on the market, yet this one has certain attractions both to the student and the surgeon. The outstanding feature is the originality and clearness of the illustrations; these are all line drawings and they are uniformly excellent. Clear and distinctive black-and-white drawings take a lot of beating. There are no half-tones or coloured illustrations in this book and this is an admirable characteristic and produces uniformity.

In this new edition the new international anatomical nomenclature, or N.A.P., replaces the B.N.A. and its Birmingham Revision of previous editions; but where the new and the old terms differ substantially from each other, the supplanted term is given in brackets. This is a good idea, for the surgeon of to-day knows very little about the Nomina Anatomica Parisiensia, or N.A.P.

This book is essentially a practical anatomy in which the surgical aspect is stressed and the human body is considered by regions which is so useful and makes for easy reference.

We predict that this edition will prove as popular as its five predecessors.

Varied Operations. An Autobiography. By the Hon. HERBERT A. BRUCE, M.D., F.A.C.S., L.R.C.P., F.R.C.S. (Eng.). $9\frac{1}{4} \times 6$ in. Pp. $366 + xviii$, with 9 plates. 1958. Toronto: Longmans, Green & Co. $6.00.

THIS is the fascinating autobiography of one of the oldest Fellows of the Royal College of Surgeons of England. It covers in vivid summary the ninety years of Dr. Bruce's happy, useful, and highly successful life. The Prime Minister of Canada, the Rt. Hon. John Diefenbaker, P.C., writes a foreword to this book.

After qualification Bruce did a year's internship at the Toronto General Hospital, after which he became ship's surgeon on the *Empress of India* in 1893 and did five round trips in that vessel. It was while serving in this ship that he performed his first appendicectomy. Later when he obtained his English Fellowship Bruce returned to Canada as Associate Professor of Clinical Surgery in the Faculty of Medicine at Toronto. After this many years were spent in general surgery until the First World War, when he came to Europe with the Canadian forces. After the war he married and returned to surgery once more. But his ability, energy, and breadth of interest marked him for honours in public life as well, and he became Lieutenant Governor of Ontario at the age of 63 and a member of the Federal Parliament at 72.

To-day Herbert Bruce is Emeritus Professor of Surgery, and a member of the Board of Governors of the University of Toronto, and founder of the Wellesley Hospital in Toronto. For recognition of his years of public service, three universities (Toronto, Queen's, and Western Ontario) have conferred on him the degree of LL.D., and during his brilliant career as a surgeon he was a founder of the American College of Surgeons and a member of its original Board of Regents.

Le Reflux Gastro-œsophagien. By P. BLONDET, J. GAILLARD, and P. MICHAUD. $10\frac{1}{4} \times 7\frac{1}{4}$ in. Pp. 158, with 34 illustrations. 1958. Paris: Expansion Scientifique Française. 2600 fr.

THIS is a monograph written jointly by a physician, a surgeon, and a laryngologist from the Faculty of Medicine at Lyons. It gives a lucid and comprehensive account of the phenomenon of gastro-œsophageal reflux in all its aspects. The early chapters are devoted to the anatomy and physiology of the lower œsophagus and cardia, and the physiopathology of reflux. Then follows a chapter on the conditions giving rise to reflux, ranging from sliding hiatus hernia to gastrectomy and pregnancy. Endoscopic and radiological investigations are described, as well as the clinical features, which are grouped into three classes: (1) the 'gas-pouch' syndrome; (2) the hiatal ring syndrome; (3) the syndrome of reflux. The last chapter is devoted to treatment, medical (largely symptomatic and palliative), endoscopic, and surgical. It is thought that too much importance has been attached by Allison to the crural sling surrounding the œsophagus and the authors believe that the important points in operative treatment are the fixation of the œsophagus to the diaphragm so as to maintain the lowest 3 cm. within the abdomen, and the restoration and reinforcement of the fundo-œsophageal angle (of His).

It is an interesting, readable, and stimulating little book. The work of others is frequently quoted, but no references are given. Although paper-backed, it is well produced on good quality paper and the illustrations are excellent.

Pathology for Students of Dentistry. By GEORGE L. MONTGOMERY, T.D., M.D., Ph.D., F.R.S.E., F.R.F.P.S.(G.), F.R.C.P.E., Professor of Pathology, University of Edinburgh. Second edition. $8\frac{1}{2} \times 5\frac{1}{2}$ in. Pp. $307 + viii$, with 134 illustrations. 1958. Edinburgh and London: E. & S. Livingstone Ltd. 40s.

IT is not an easy matter to write a text-book on a large basic subject such as pathology for a limited profession such as dentistry. However, Professor Montgomery did this with authoritative skill in his first edition which was published in 1953. It was judged by the dental and medical profession as a truly excellent little book, well written and beautifully produced.

The new second edition is even better and the chapter on the causation of tumours has been rewritten.

The dental student of to-day will ever be thankful to Professor Montgomery for this most interesting and most readable of books.

Lehrbuch der Chirurgie. Edited by H. HELLNER, R. NISSEN, and K. VOSSSCHULTE. $10 \times 6\frac{3}{4}$ in. Pp. $1112 + xxxvi$, with 652 illustrations. 1958. Stuttgart: Georg Thieme. D.M. 84.

THE second edition of this text-book has appeared within sixteen months of publication of the prototype. Its contributors are drawn from all the German-speaking countries, and include an expatriate holding the Chair of Surgery in Alexandria, Egypt. One of the editors practised for many years in the U.S.A.

The book adheres to the now familiar American pattern of surgical texts. Matters of general interest are considered first, followed by a systematic regional survey.

Great importance is attached to the exposition of applied physiology, but an account of regional anatomy, as prescribed by convention, is retained. Interesting historical notes precede discussion of clinical features, methods of investigation, and indications for surgery. No attempt is made to go into operative details beyond instancing the rationale of relevant procedures.

The chapter on tumours, so often monotonously descriptive, confines itself to the fundamentals of oncology, but also reviews the principles of diagnosis and treatment in the light of current practice. Both the contribution on radio-active isotopes and the chapter on metabolic responses to surgery are timely as well as impressive. Thrombosis and embolism are dealt with provocatively.

Some outstanding regional chapters include those concerned with the endocrines, the heart and lungs, the abdomen, and the skeletal system. The book concludes with an unusual feature, devoted to the assessment of orthopædic disabilities for compensation purposes.

The orientation of the text is thoroughly up to date. This is underlined by the topicality of the literature referred to, which is commendably international. The illustrations are well chosen, and of a high standard throughout.

A few printing errors (J. W. Mayo—p. 627; proctitis—p. 659), and the granting of American citizenship (Hon.) to Russell Brain in the section dealing with the

carpal-tunnel syndrome, are trivialities only mentioned to facilitate their correction in a future edition.

This sort of book sounds the death-knell of the unreasoned, undocumented account, based primarily on pathological anatomy, which was the undergraduate student's main surgical stand-by until quite recently. British publishers, and especially those interested in exporting their wares to the Scandinavian and other uncommitted markets, should take cognizance of this excellent work.

Textbook of Surgery. Edited by GUY BLACKBURN and REX LAURIE. Pp. 1122, fully illustrated. 1958. Oxford: Blackwell Scientific Publications. 84s.

ANOTHER text-book of surgery! Is there possibly room for it? The answer in this case is certainly 'Yes', for this present work is the product of the staff of Guy's Hospital and it portrays the teaching and operative technique as carried out there.

This text-book has been written for the undergraduate student and it certainly covers the field of surgery in an excellent manner. Any student who masters this volume should not have any difficulty in the final surgical examinations wherever they may be conducted.

Although this is a multi-author book the editors have supervised their work well, for there is very little overlapping in the various fields of surgery. The illustrations as a whole are good, especially the line drawings, but one or two are a little difficult to understand—for instance, Fig. 7 on page 625 is supposed to be an intussusception, but at first sight it looks like fibroids in a uterus. However, this is a slight criticism on an otherwise excellent book.

We would like to congratulate Mr. Guy Blackburn and Mr. Rex Laurie on a great achievement.

Callander's Surgical Anatomy. By BARRY J. ANSON, M.A., Ph.D. (Med. Sc.), Chairman, Department of Anatomy, and Robert Laughlin Rea Professor, Northwestern University Medical School and Member of Staff, Passavant Memorial Hospital; and WALTER G. MADDOCK, M.S., M.D., F.A.C.S., Edward S. Elcock Professor of Surgery, Northwestern University Medical School. Fourth edition. 10×7 in. Pp. 1157+xviii, with 1047 illustrations. 1958. Philadelphia and London: W. B. Saunders Co. 147s.

THE fourth edition of this well-known book has been thoroughly revised and many new illustrations have been incorporated. New operative techniques have been added and the whole comprehensive work covers the immense field of surgical anatomy.

The great feature of this book is the abundance and the excellence of the illustrations, many of which are original.

The demand for a fourth edition so soon after the third reflects the popularity of this work.

Leistungen und Ergebnisse der Neuzeitlichen Chirurgie. By EMIL K. FREY. 10½×7¼ in. Pp. 339+xii, with 154 illustrations. 1958. Stuttgart: Georg Thieme Verlag. D.M. 84.

THIS collection of surgical essays was written in order to celebrate the seventieth birthday of Professor Frey, the eminent German surgeon, who is perhaps best known abroad by his *Cardiac Surgery*, which he wrote in 1956 with the collaboration of Kuetgens.

The title of the present book could probably best be translated *Recent Advances in Surgery*, and the idea has been to confirm one of Professor Frey's favourite opinions, that new discoveries in surgery should prove themselves in actual clinical practice.

The resulting 38 articles written by various authors, who are all either friends or surgical offsprings (or perhaps both) of Frey's, are grouped in seven sections: anæsthetics, cardiovascular, neurological, thoracic, abdominal, urological, and orthopædic surgery.

The editor has tried to collect articles that are of common interest and many matters of practical importance are discussed. Yet the nature of the contributions differs, some articles giving general reviews (e.g., Nissen on gastric surgery), others discussing the results of established procedures (e.g., Mason on the surgical closure of the ductus arteriosus), and still others dealing with subjects that are more or less experimental (as the five articles on kalikrein or padutin—the drug discovered by Frey which is nowadays widely used in the treatment of occlusive arterial disease in Germany).

It is not possible to mention here all the separate contributions; the whole has become an attractive looking and very interesting demonstration of the high standard German-speaking surgeons have once more set. Those knowing Professor Frey personally will most certainly want to possess their own copy of this book.

The Preservation of Eyesight. By Sir ARTHUR S. MACNALTY, K.C.B., M.A., M.D., F.R.C.P., F.R.C.S., formerly Chief Medical Officer of the Ministry of Health and Ministry of Education. 8½×5½ in. Pp. 107+vi. 1958. Bristol: John Wright & Sons Ltd. 12s. 6d.

THIS is a useful little monograph which sets out in a clear way the common affections of the eye, the causes of temporary loss of sight, and blindness. It is interesting to note that as far back as 1616 a brief treatise on the preservation of the eyesight was written by Walter Bailey, but since that date no book exists which recounts in simple language the care and precautions necessary to maintain and keep good eyesight.

This present monograph should prove invaluable to student, busy practitioner, and optician.

A Practice of Thoracic Surgery. By A. L. D'ABREU, O.B.E., Ch.M., F.R.C.S., Surgeon, Queen Elizabeth Hospital, Birmingham. Second edition. 9¾ × 7 in. Pp. 619 + viii, fully illustrated. 1958. London: Edward Arnold (Publishers) Ltd. 100s.

IT is only five short years since the first edition of this authoritative work on thoracic surgery was published, and we then considered it an excellent monograph.

This new edition is a worthy successor of the former and the author has been able to bring the text completely up to date. There is considerable new matter dealing with the surgery of the heart and great vessels, also with the surgery of cancer of the lung.

There can be little doubt that this book will prove of real value not only to surgeons who have to operate on the thorax, but to those, and these are an increasing number, who make use of a thoraco-abdominal approach to the upper abdomen.

The postgraduate student who is preparing for some of the higher degrees or diplomas will find this book invaluable.

Outline of Fractures. By JOHN CRAWFORD ADAMS, M.D., F.R.C.S., Consultant Orthopaedic Surgeon, St. Mary's Hospital, London. Second edition. 8½ × 5½ in. Pp. 268 + viii, with 237 illustrations. 1958. Edinburgh and London: E. & S. Livingstone Ltd. 27s. 6d.

WITHIN two years of its first appearance a second edition of this book indicates its popularity. Written dogmatically for medical students, practitioners and physiotherapists,

it contains much sound advice such as, "No longer is it accepted automatically that because the bone fragments are not in exact apposition manipulation must be carried out", while a striking simile, such as, "the spinal cord . . . soft and friable like the soft roe of a herring", is arresting. Throughout the book attention is directed to the need of the preservation and restoration of function and the importance therefore of giving proper consideration to the soft parts and the joints related to the broken one. Fractures of the skull, face, and jaw are omitted, but the spine and pelvis are included and there is a good over-all account of the commoner fractures of the rest of the skeleton. Illustrations are both lavish and clear, the reproduction of X-ray films being excellent, and along with a very readable and clear text these make this an attractive guide which can be confidently recommended.

BOOK NOTICES

[The Editorial Committee acknowledge with thanks the receipt of the following volumes. A selection will be made from these for review, precedence being given to new books and to those having the greatest interest to our readers.]

Lesions of the Lower Bowel. By RAYMOND J. JACKMAN, M.D., M.S. in Proctology, Section of Proctology, Mayo Clinic, and Associate Professor of Proctology, Mayo Foundation, Graduate School, University of Minnesota. 9×6 in. Pp. 347+xxxviii, with 56 illustrations. 1958. Springfield, Ill.: Charles C. Thomas. (Oxford: Blackwell Scientific Publications.) £5 17s. 6d.

Cancer of the Pharynx, Larynx and Œsophagus and its Surgical Treatment. By RONALD W. RAVEN, O.B.E. (Mil.), T.D., F.R.C.S., Joint Lecturer in Surgery, Westminster Medical School, University of London. 9½×6½ in. Pp. 286+xiv, with 189 illustrations. 1958. London: Butterworth & Co. (Publishers) Ltd. 67s. 6d.

Brain Memory Learning. By W. RITCHIE RUSSELL, C.B.E., M.D. (Edin.), D.Sc. (Oxon.), F.R.C.P. (Edin. and Lond.), Lecturer in Neurology, University of Oxford. 8½×5½ in. Pp. 140+xii, with 12 illustrations. 1959. Oxford: Clarendon Press. 18s.

Illustrated Pre-operative and Post-operative Care. By PHILIP THOREK, M.D., F.A.C.S., F.I.C.S., Professor of Surgery, Cook County Graduate School of Medicine. 9×6 in. Pp. 98+xii, with 60 illustrations. 1959. London: Pitman Medical Publishing Co. Ltd. 30s.

Injuries and Surgical Diseases of the Ischium. By HENRY MILCH, M.D., Attending Orthopedic Surgeon, Hospital for Joint Diseases, New York. 10×6½ in. Pp. 163+x, with 106 illustrations. 1959. London: Pitman Medical Publishing Co. Ltd. £4 4s.

Surgical Convalescence. Edited by F. CURTIS DOHAN. 9×6 in. Pp. 157, illustrated. 1958. New York: New York Academy of Sciences. $4.00.

Third Tissue Homotransplantation Conference. Edited by BLAIR O. ROGERS. 9×6 in. Pp. 359, fully illustrated. 1958. New York: New York Academy of Sciences. $5.00.

Contributions of the Physical, Biological and Psychological Sciences in Human Disability. Edited by RENATO CONTINI. 9×6 in. Pp. 160, illustrated. 1958. New York: New York Academy of Sciences. $3.50.

Enzymes in Blood. Edited by LAURENS P. WHITE. 9×6 in. Pp. 384, fully illustrated. 1958. New York: New York Academy of Sciences. $5.00.

The Basic and Clinical Research of the New Antibiotic Kanamycin. Edited by MAXWELL FINLAND. 9×6 in. Pp. 391, illustrated. 1958. New York: New York Academy of Sciences. $5.00.

Re-education of the Injured Shoulder. By R. BARRIE BROOKES, F.C.S.P., Rehabilitation Officer, Birmingham Accident Hospital. 8½×5½ in. Pp. 114+viii, with 59 illustrations. 1959. Edinburgh and London: E. & S. Livingstone Ltd. 12s. 6d.

Autopsy Diagnosis and Technic. By OTTO SAPHIR, M.D., Clinical Professor of Pathology, University of Illinois Medical School, Chicago. Fourth edition. 7½×5 in. Pp. 549+xxiv, with 80 illustrations. 1958. London: Cassell & Co. 63s.

Genetic Concept for the Origin of Cancer. Edited by LEONELL C. STRONG. 9×6 in. Pp. 434; fully illustrated. 1958. New York: New York Academy of Sciences. $5.00.

Lymphocytes and Plasmacytes in Nucleoprotein Metabolism. By MARGARET A. KELSALL and EDWARD D. CRABB, Department of Biology and Research Service Laboratories, University of Colorado. 9×6 in. Pp. 45. 1958. New York: New York Academy of Sciences. $2.00.

The Neurologic Examination. By RUSSELL N. DE JONG, M.D., Professor of Neurology and Chairman of Department of Neurology, University of Michigan Medical School. Second edition. 9¾×6¾ in. Pp. 1078+xv, with 368 illustrations. 1959. London: Pitman Medical Publishing Co. Ltd. £7.

British Surgical Practice. Surgical Progress 1958. Edited by Sir ERNEST ROCK CARLING, LL.D., F.R.C.S., F.F.R., Honorary Consulting Surgeon, Westminster Hospital; and Sir JAMES PATERSON ROSS, K.C.V.O., LL.D., M.S., P.R.C.S., F.R.A.C.S., F.A.C.S., Surgeon and Director of Surgical Clinical Unit, St. Bartholomew's Hospital, London. 9¾×6½ in. Pp. 441+x, with 98 illustrations and fully indexed. 1958. London: Butterworth & Co. (Publishers) Ltd. 52s. 6d.

Operative Surgery. Progress Volume 1958. Edited by CHARLES ROB, M.C., M.Chir., F.R.C.S., Professor of Surgery, St. Mary's Hospital, London; and RODNEY SMITH, M.S., F.R.C.S., Surgeon, St. George's Hospital, London. 10¾×8¼ in. Pp. 100+xiv, fully illustrated, and with the Indices to volumes 1–8. 1958. London: Butterworth & Co. (Publishers) Ltd. 60s.